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Volume 27, issue 4

Canadian Medical Association

Volume 27, No. 4, July 1984

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The Canadian Journal of Surgery

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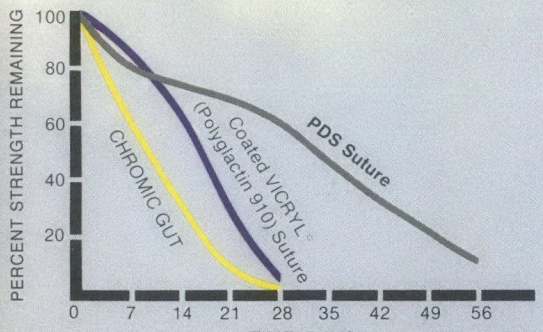

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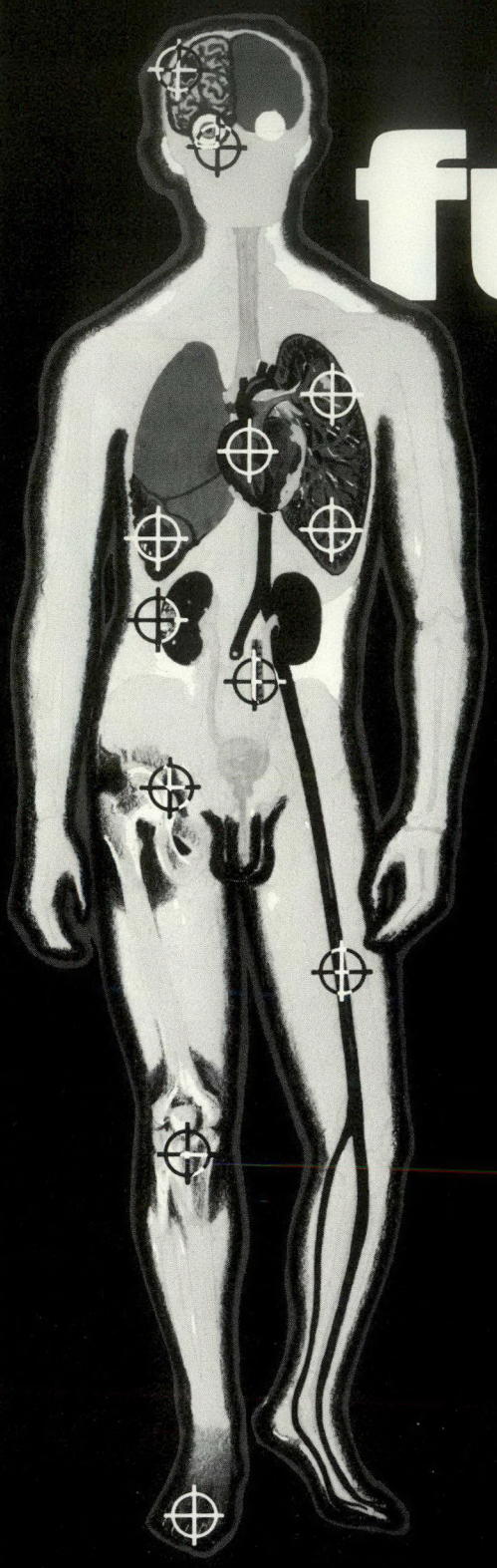

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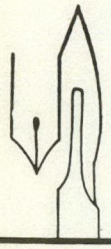
QUILL ON SCALPEL

This section provides a medium through which Canadian surgeons can declare themselves, briefly and informally, on the day-to-day affairs of surgery.



Highly Selective Vagotomy: Forward or Backward in the Surgical Treatment of Duodenal Ulcer?

How many major advances have been made in gastrointestinal surgery since the introduction of vagotomy by Dragstedt? Regrettably, the answer is dismally few. The great increase in our understanding and knowledge of the pathophysiology of many diseases unfortunately has not been translated into many important new operations. Surgical results have certainly improved, but this can be attributed to better selection of patients and more sophisticated care pre- and postoperatively. Gastrointestinal surgeons today are doing essentially the same operations as the surgeons of the previous generation.

When Johnston and Wilkinson[1] and Amdrup and Jensen[2] independently suggested an entirely new approach to vagotomy, based on the physiologic experiments of Griffith and Harkins,[3] there was considerable excitement. Highly selective vagotomy, by preserving the vagal branches to the antrum, allowed the surgeon to dispense with the drainage procedure that appears to be an essential addition to complete gastric vagotomy. The advantages were recognized immediately. Because the gastrointestinal tract is not entered, the operation is much safer. As no drainage procedure is performed, there are fewer long-term side effects. The only apparent disadvantage is that the operation, if done properly, takes longer to perform than a standard vagotomy with a drainage procedure. The one remaining question, therefore, was the rate of recurrent ulceration.

The initial recurrence rate following highly selective vagotomy was not only as low as but even lower than after vagotomy and drainage.[4] These results were treated with skepticism by some, who wondered how fewer recurrences could be achieved with the same degree of acid reduction. There was anxiety about the conversion of almost all patients from insulin-test negative results to insulin-test positive. There was concern about the possibility of reinnervation from the antrum. However, many surgeons and the majority of gastroenterologists, particularly in Europe, hailed this new operation as a major advance in the treatment of duodenal ulcer. Enthusiasts advocated its use not only for uncomplicated duodenal ulcer but also for duodenal ulcers complicated by pyloric obstruction, perforation or hemorrhage, for gastric ulcer, hiatus hernia and other conditions. An operation with so little attendant morbidity was hard to eschew. Has it stood the test of time? As recently as 1980, no less an authority than the late Dr. Morton Grossman was warmly endorsing it and advocating its wider use in the United States.[5]

In this issue (pages 340 and 341) Mr. Terence Kennedy reports on 512 highly selective vagotomies performed over 15 years by a number of surgeons. There was only one operative death and a proven recurrence rate of 13% in those followed

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Instructions to Contributors

Detailed instructions to contributors, in English and French, appear on page 83 of the January 1984 issue.

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up for more than 5 years. That record is impressive and is more convincing than the reports of spectacular results obtained by a single surgeon. What we need to know is whether highly selective vagotomy should be recommended as the best elective surgical treatment for all patients with duodenal ulcer.

It is ironic that the strongest claim for this operation (unsupported by any control data) comes from the surgical department that so elegantly demonstrated the feasibility and value of the prospective, randomized, controlled surgical trial.[6] It is also worth recalling that the proven recurrent ulcer rate after vagotomy and drainage in that trial, involving many surgeons, was only 2.5%. Kennedy states that there are no published randomized controlled data comparing highly selective vagotomy with truncal vagotomy and drainage, with a follow-up of 5 years or more. To the shame of the surgical community, this is strictly true. But we are not entirely without good data. There have been several controlled trials. Madsen and Kronborg[7] compared the results of highly selective vagotomy with selective vagotomy and pyloroplasty after 5½ to 8 years and found ulcer recurrence rates of 26% and 14%, respectively. Elder and colleagues[8] in this Journal reported a randomized trial of highly selective vagotomy versus truncal vagotomy and pyloroplasty in which the mean follow-up was 4 years. The rate of recurrent ulcer following highly selective vagotomy was 21.4% compared with 7.5% following vagotomy and pyloroplasty. Surprisingly, there was no difference in the incidence of any side effect other than diarrhea. Koo and associates[9] compared highly selective vagotomy with truncal vagotomy and drainage after a median follow-up of 4 years. Recurrence after highly selective vagotomy was 18% and after vagotomy and drainage was 12%. Christiansen and associates[10] reported a 2- to 5-year follow-up of highly selective vagotomy compared with truncal vagotomy and drainage and selective vagotomy and drainage. The risk of ulcer recurrence calculated by an actuarial method was significantly higher after highly selective vagotomy than after truncal vagotomy and drainage but not after selective vagotomy and drainage. One of the most worrisome features is that recurrent ulceration after vagotomy and drainage occurs within 2 years or probably not at all, whereas after highly selective vagotomy it is apparent that the longer the patients are followed the more recurrent ulcers are detected. The Leeds group[11] has progressively increased its reported recurrence rate after highly selective vagotomy from 0% to 11%. At what point will recurrent ulcers stop appearing? The true recurrence rate of 35% after gastroenterostomy alone was not recognized for more than 20 years.

None the less, some surgeons, armed even with these facts, strongly advocate highly selective vagotomy as the primary operation for duodenal ulcer for two reasons. First, recurrent ulcer can now be treated successfully with powerful H_2 blocking agents and second, if worse comes to worst, the patient can be offered another operation. The reason the patient was offered an operation in the first place was because we do not accept that lifetime treatment with H_2 blocking agents is appropriate for duodenal ulcer disease. How safe and effective vagotomy and antrectomy (the operation generally recommended) will prove to be for failed highly selective vagotomy is not yet known. But is it reasonable to offer an operation that even one of its originators predicts will fail within 10 years 23% of the time?[12] The ultimate defence of highly selective vagotomy, of course, is the claim that if the operation is done properly, the recurrence rate will not be 23% but 2% to 6%. If the operation is so difficult to do correctly, should it be advocated for general use? Why has there been no report of long-term, independent, objective follow-up with such respectable recurrence rates? Why have several interim reports[13-15] of controlled trials of highly selective vagotomy, including one by Kennedy and associates, not been followed by the publication of detailed long-term results?

Those who stubbornly promote the *concept* that highly selective vagotomy is not only safer but is followed by fewer sequelae and a similar number of recurrent ulcers as vagotomy and drainage must face the *facts*. Facts come only from properly controlled prospective trials with lengthy follow-up.

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Accuracy of Noninvasive Peripheral Arterial Testing

Evaluation of peripheral arterial disease by noninvasive methods has played an increasingly important role in patient management as noted by Symes and colleagues in this issue (pages 345 to 347). The clinical impression of arterial status is complemented by the objective, quantitative evaluation of noninvasive testing. Scientific evaluation of peripheral arterial disease or procedures requires laboratory confirmation and noninvasive studies may be able to provide information not available even by arteriography, thus increasing the accuracy of diagnosis.

The accuracy of a noninvasive technique (true positive plus true negative results divided by the total number of examinations) varies depending on the patient population studied. Accuracy also depends on the threshold level chosen for a positive test, which can vary according to whether one is more concerned with detection of patients with disease (sensitivity) or excluding those without disease (specificity). Assessment of accuracy also requires a proper "gold" standard for comparison.

With respect to peripheral arterial disease, the accuracy of clinical diagnosis alone may be very high. Baker and associates[1] compared clinical evaluation by attending surgeons with noninvasive laboratory testing (segmental pressures, femoral Doppler recordings without spectrum analysis and treadmill exercise) of 102 patients. A similar, high degree of accuracy was obtained from both the noninvasive studies and the attending surgeon, who was correct in 98 patients and at least partially correct in the other 4. The less-experienced clinicians (surgical housestaff), however, did not fare as well, with only 62% totally correct anatomic diagnoses. The high degree of accuracy of the attending surgeon in this study may have been influenced by the patient population selected since all 102 patients were admitted to hospital for arteriography and thus likely had severe disease which often facilitates clinical accuracy. The patients in whom diagnosis is more difficult are those who have disease in both iliac and femoral systems. Several different methods have been used to detect combined segment disease. The technique of combined segmental pressure measurements and pulse-volume recordings was developed by Raines and associates.[2] Segmental pressures at the common femoral level are difficult to measure since it is not possible to place the thigh pressure cuff high enough. Combined segmental pressure measurement and pulse-volume recording may not accurately predict the major contributing lesion in combined segment disease.[3] A study is currently in progress at the Miami Heart Institute to define the accuracy and limitations of this method in combined segment arterial disease.[3]

The other technique of noninvasive testing evaluated by Symes and associates was Doppler waveform analysis using continuous wave Doppler ultrasound and a spectrum analyser with calculation of pulsatility index. This may help in difficult cases, where the patient has combined disease. Johnston and associates,[4] using a pulsatility index of 5.5 as a threshold level, found 95% sensitivity and specificity in detecting hemodynamically important aortoiliac disease (corresponding to a resting aortofemoral pressure gradient of 10 mm Hg). Other investigators have been less optimistic regarding the accuracy of the pulsatility index in diagnosing iliac disease,[5,6] but their techniques differed in a major fashion from that of Johnston and colleagues.

The lack of a definite "gold" standard makes comparison of various techniques difficult. The inadequacy of single-plane arteriography to define hemodynamically important aortoiliac disease has long been appreciated.[7] Some have used aortofemoral pressure gradients as the "gold" standard of iliac disease at rest[4] and after vasodilatation by papaverine.[8]

Noninvasive studies play a major role in the management of the vascular patient. Either combined segmental pressure measurement and pulse-volume recording or Doppler waveform analysis may be adequate in the majority of patients. In more complicated cases where there is combined iliac and femoral disease, evidence that combined segmental pressure measurement and pulse-volume recording allows precise anatomic diagnosis is not available. While controversial, preliminary evidence suggests that Doppler waveform analysis may facilitate diagnosis of combined segment disease and give information in addition to that supplied by single-plane arteriography.[4] In the occasional difficult case of multilevel disease, even a combination of clinical, noninvasive and arteriographic methods may not give an accurate hemodynamic diagnosis and direct aortofemoral pressure measurements may be required. The comparison of accuracy of noninvasive techniques in vascular disease is difficult because of the variability of patient populations and lack of a suitable "gold" standard.

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Simplified Dressing for the Drained Empyema

Any empyema, complicated or not by a bronchopleural fistula, must be drained by a closed or open technique. Care of the wound imposes a heavy burden on medical and paramedical staff and discomfort to the patient is severe. The pleural abscess releases a large volume of infected secretions that not only irritate the skin around the drain site but are a constant source of reinfection. Frequent dressing changes, costly in time and material, are required and cannot be done on an outpatient basis. Moreover, prolonged bed rest and inactivity delay the recovery of these patients, who are already severely debilitated, and increase the risks of additional complications. Our experience with enterostomy therapy gave us the opportunity to design a closed system technique that eliminates most of these inconveniences.

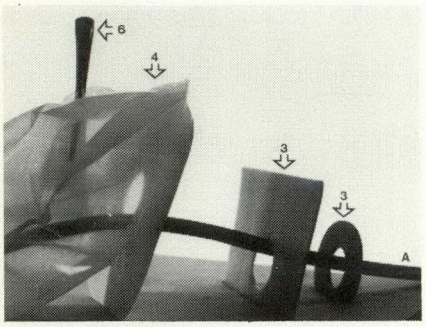

FIG. 1—Material required: A = pleural drain, 3 = skin barrier washer and square, 4 = bag, 6 = vent.

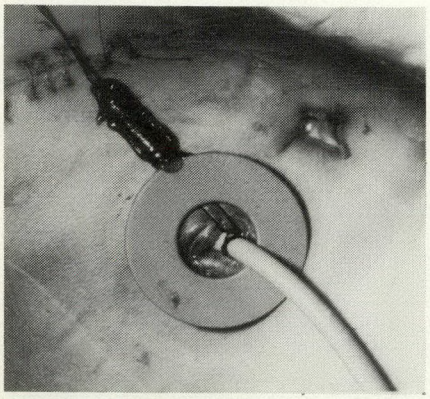

FIG. 2—Drain with its anchor line and skin barrier washer.

Technique

The purpose is to assure the total collection of the purulent secretions into a bag without spillage, skin irritation or air trapping (Fig. 1). First, the skin around the drain or the edges of the window is cleaned and covered with a layer of waterproof protective coating (United Skin Prep., United, Division of Howmedica Inc., Guelph, Ont.) that will enhance the holding power of the dressing. If the pleural drain must be kept in place, stitching must be avoided since it is painful and will eventually cut through the skin. Therefore, the drain is cut 4 cm from the thoracic wall and a heavy silk is tied around it; then its free end is glued to the skin with a thin layer of Karaya paste (Hollister Inc., Willowdale, Ont.). Next, a round washer of skin barrier (Hollister Inc.) is applied around the edges of the wound (Fig. 2) and is covered with an adhesive blanket (10 × 10 cm) of the same material (Fig. 3). The inside edge of the wound is sealed with additional Karaya paste to assure a watertight barrier. A urinary diversion bag (Hollister Inc.) is glued to the skin barrier patch. Further adhesion of the bag is guaranteed by a layer of Micropore Surgical Tape (3M Canada Inc., London, Ont.) applied to its external base. In the presence of a bronchial fistula, venting of the bag is assumed by a no. 14 French rubber drain (Robi-Nel Catheter, Argyle, Division of Sherwood Medical Industries Ltd., St. Louis, Mo.) introduced through its upper part and sealed with some tape (Fig. 4). The only care needed will then be the emptying of the bag as required. Inspection of the wound, irrigation or bacterial culture can be done through the fundus of the bag. On an outpatient basis, periodic controls may be extended to 10 to 15 days.

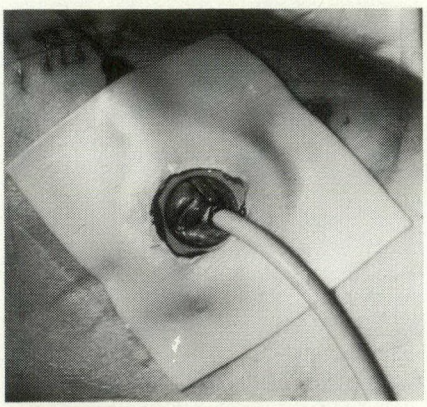

FIG. 3—Skin barrier square.

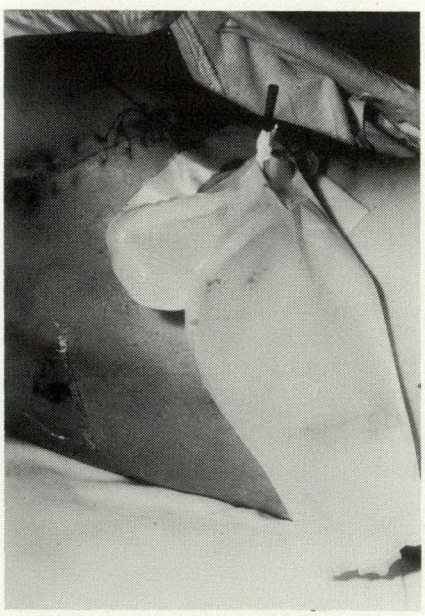

FIG. 4—Final set up: sealed vented bag

In our experience, this method has simplified the treatment of drained empyema. By eliminating the constant pain and the anguish of a dirty weeping wound and by permitting the patient an early return home to normal activities, it has brought about the essential elements of a quick recovery and cut down considerably on hospital costs.

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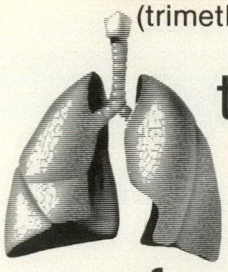

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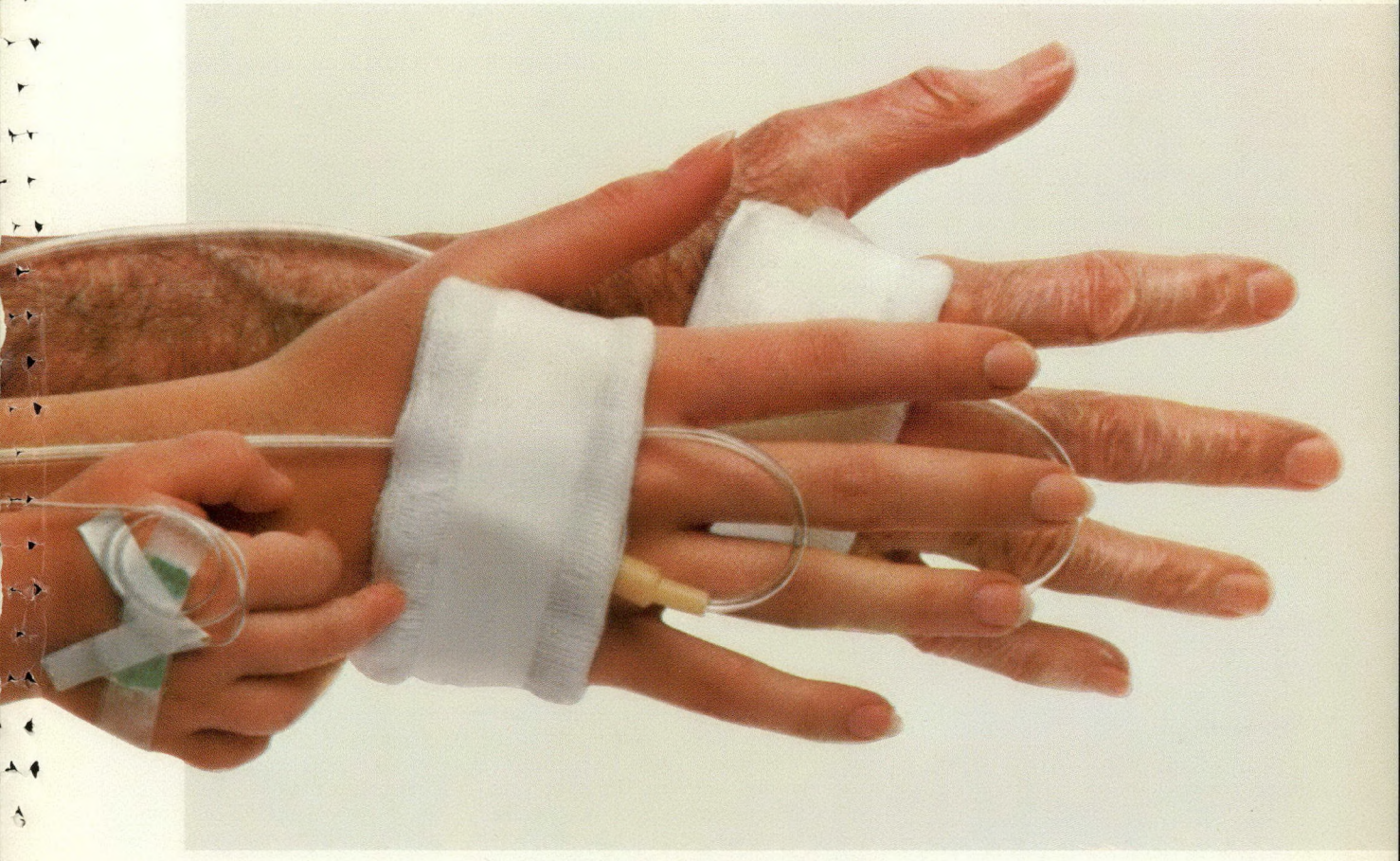

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CORRESPONDENCE

Contributions to the Correspondence section are welcomed.
They should be typewritten and double spaced.

Operative Myocardial Protection

To the editors.—I would like to compliment Brown and Chiu on their excellent paper "Operative myocardial protection: does an elevated level of creatine phosphokinase-MB isoenzyme always indicate myocardial necrosis?" (*Can J Surg* 1984; 27: 80–3). Their answer in the negative and their careful documentation of methods used, with myocardial needle biopsy confirming the lack of extensive infarction, puts the routine measurement of creatine phosphokinase-MB isoenzyme postoperatively into its proper perspective as a quality control factor. Their myocardial temperature threshold of 25°C is certainly higher than I would accept,[1] but their excellent clinical results cannot be faulted. Eight years ago I also reported a minimal effect of the duration of cross-clamping on creatine phosphokinase-MB isoenzyme peak values,[2] but we did not perform the frequent analyses that make Brown and Chiu's study superior. I think the explanation for why patients who undergo valve replacement have higher levels of enzyme release than those who undergo coronary artery grafting is covered by the authors' formula on page 82. Certainly, in most patients with aortic valve disease and in many patients with mitral insufficiency, the myocardial mass at risk is markedly increased, compared with that in the average patient with coronary artery disease.

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Small-Bowel Varices

To the editors.—Drs. Ostrow and Blanchard, in the discussion of their most interesting paper on bleeding small-bowel varices (*Can J Surg* 1984; 27: 88–9), indicate that only a few similar cases have been reported. I should like to report briefly another patient with a bleeding small-bowel varix.

A 16-year-old girl had had a ruptured appendix with peritonitis when she was 1 year old. It was satisfactorily treated and she had no further complications for 4 years when she was discovered to have Banti's syndrome and underwent splenectomy. Apparently the cavernous transformation of the portal vein was unrecognized.

When the patient was admitted, she gave a history of passing tarry stools for several days but without hematemesis. A nasogastric tube introduced into the stomach did not produce blood and subsequently an upper gastrointestinal series was reported as "unremarkable". She continued to pass blood and required transfusion, so abdominal exploration was elected. The stomach, duodenum and liver appeared normal. On examination of the small bowel, a loop was found adhering to the back of the previous laparotomy incision. A large vein could be seen running through the mesentery across one side of the small intestine, entering the abdominal wall near the umbilicus. The rest of the small intestine did not appear abnormal but distally was distended with blood.

The varix was ligated in the mesentery and the small intestine dissected from the abdominal wall. The vein entering the abdominal wall was suture-ligated and the wound closed.

Subsequently, the patient did well and in the 2 years of follow-up had no further bleeding episodes. She was subsequently lost to follow-up so her ultimate fate is unknown.

At operation there was no evidence of multiple intramural jejunal varices but only one large varix. The previous splenectomy with the resultant small-bowel adhesion to the abdominal wall apparently established a vascular connection between the portal and systemic venous system that resulted in variceal hemorrhage at the jejunal level. It therefore appears possible that in any patient with uncorrected portal hypertension, whether due to hepatic or prehepatic obstruction, varices may develop at anomalous sites, with hemorrhage, particularly if there has been previous peritonitis or abdominal surgery and adhesions are present.

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Lymphoscintigraphy for Staging Breast Cancer

To the editors.—In his editorial, "Lymphoscintigraphy in the staging of breast cancer" (*Can J Surg* 1983; 26: 487–8), Shibata has obscured the simple facts we presented. Our study (*Can J Surg* 1983; 26: 507–9) demonstrated that axillary lymphoscintigraphy in its present state of development is not a reliable indicator of axillary lymph-node metastases. It is, however, worth further study. We also prospectively tested the specificity of preoperative internal mammary lymphoscintigraphy because of the possibility that postoperative surgical artefact had confounded the data on which Ege and Clark based their original conclusions.[1] Only one false-positive result was obtained in the preoperative examination of 76 patients with breast masses that were subsequently proven to be noncancerous. There is no doubt that the test is remarkably specific for nonmalignant disease. The suggestive correlation of the abnormal preoperative internal mammary scan with the most sensitive biologic marker presently in use (involved axillary nodes) and with recognized anatomical lymphatic drainage pathways (medial and

central location of the primary tumour in the breast) may be purely coincidental. Surgical excision of the whole internal mammary lymph-node chain should be performed to settle the question. Unfortunately, this is not ethically justifiable. Alternatively, we need large numbers of patients and long-term follow-up. We do not believe we have enough evidence to start adjuvant therapy on the basis of an abnormal internal mammary lymphoscintigram in patients with negative axillary nodes. We do believe this part of the study is worth continuing.

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Esophagopericardial Fistula Producing Purulent Pericarditis

To the editors.—In a recent review, Cyrlak and associates[1] reported what they thought was the 50th documented case of esophagopericardial fistula. They noted that such fistulas are uncommonly related to operation and when they occur postoperatively they are recognized clinically within 2 years. We report a patient who had esophagopericardial fistula, documented radiologically, and presented 22 years after repair of a lower esophageal stricture.

An 81-year-old woman was admitted suffering retrosternal chest pain, which had been present for 12 hours. Twenty-two years earlier she had undergone excision of a benign lower esophageal stricture with interposition of a jejunal loop between the distal esophagus and stomach (Merendino procedure[2]). Her heart rate was 115 beats/min, temperature was 37°C and blood pressure 90/70 mm Hg with a paradoxical pulse pressure of 30 mm Hg; Kussmaul's sign was present. The heart sounds were soft and no pericardial rub was audible. The findings on abdominal examination were unremarkable. The leukocyte count was 30×10^9/L. There was elevation of the ST-segment in the lateral leads. Chest roentgenogram revealed an enlarged, globular cardiac silhouette. A two-dimensional echocardiogram showed a large pericardial effusion.

Pericardiocentesis was performed and an indwelling catheter left for pericardial drainage. The leukocyte count in the pericardial fluid was 74×10^9/L; there was a predominance of neutrophils. Gram-positive cocci and gram-negative bacilli were present on the smear. Cultures subsequently grew *Staphylococcus aureus,* α-hemolytic *Streptococcus* and *Clostridium perfringens.* Roentgenogram after a swallow of dilute meglumine diatrizoate demonstrated a free passage from the jejunal interposition graft to the pericardial space. Esophagogastroduodenoscopy demonstrated a stomal ulcer at the gastrojejunal anastomosis. The fistula was not visualized.

After 2 weeks of pericardial drainage, parenteral feeding and intravenously administered penicillin, netilmicin and metronidazole, her clinical status was unimproved. Excision of the interposition graft and fistula was performed. Wide pericardial to pleural cavity drainage was achieved and esophagogastric reconstruction was performed. Her postoperative course was complicated by septicemia and acute renal failure. The patient died 7 weeks after admission. Autopsy revealed evidence of extensive pericarditis and *Candida albicans* was isolated from the pericardial sac.

Development of esophagopericardial fistula as late as 22 years after operation has not been reported before. Purulent pericarditis in our elderly patient is typical in many ways of the changed spectrum of purulent pericarditis in the antibiotic era. The general incidence of purulent pericarditis has declined since 1944 and its occurrence has become relatively more common in adults, in women and following thoracic surgery.[3] Fever is seldom absent; in the series of Rubin and Moellering[4] only 4% of patients had no fever. Anaerobic and aerobic gram-negative bacteria are being recognized more frequently in this infection.[5]

The overall mortality for patients with purulent pericarditis who are treated is about 40% and when unrecognized the disease is almost always fatal.[3] Although the diagnosis of purulent pericarditis is undoubtedly facilitated by the use of two-dimensional echocardiography, the unexpected, fatal, late postoperative complication in our patient underscores the need for acute awareness of the condition.

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Perforated Duodenal Ulcer

To the editors.—In response to the letters of Cohen and Fong (*Can J Surg* 1984; 27: 7), I wish to make the following comments. Perforation is a complication of duodenal ulcer. Fortunately, with specific drugs, peptic ulcer disease is not as common as it was. Once they have undergone plication, 30% to 50% of patients continue to enjoy a trouble-free life. Surgery for perforation should be *safe,* simple, soon and just sufficient for the immediate problem.

Definitive surgical treatment for peptic ulcer disease should be offered after a medical regimen has failed, after biopsy of the ulcer has been obtained, after basal acid output and maximal acid output have been studied, after the gastrin level has been ascertained and associated disease has been ruled out. The patient should be informed of the recurrence rate of 5% to 7% after vagotomy and drainage and of the crippling long-term effects on nutrition and quality of life of adding hemigastrectomy.

Dr. Jordan of Baylor University advocates a drastic solution to a simple problem — a "no mortality" treatment is preferable to "accepted mortality" — by being overly aggressive.

In socioeconomically backward areas where patient compliance is not ensured, definitive treatment as the initial treatment for perforation is not to my mind academic or catholic in the case of a disease whose etiology is still not known.

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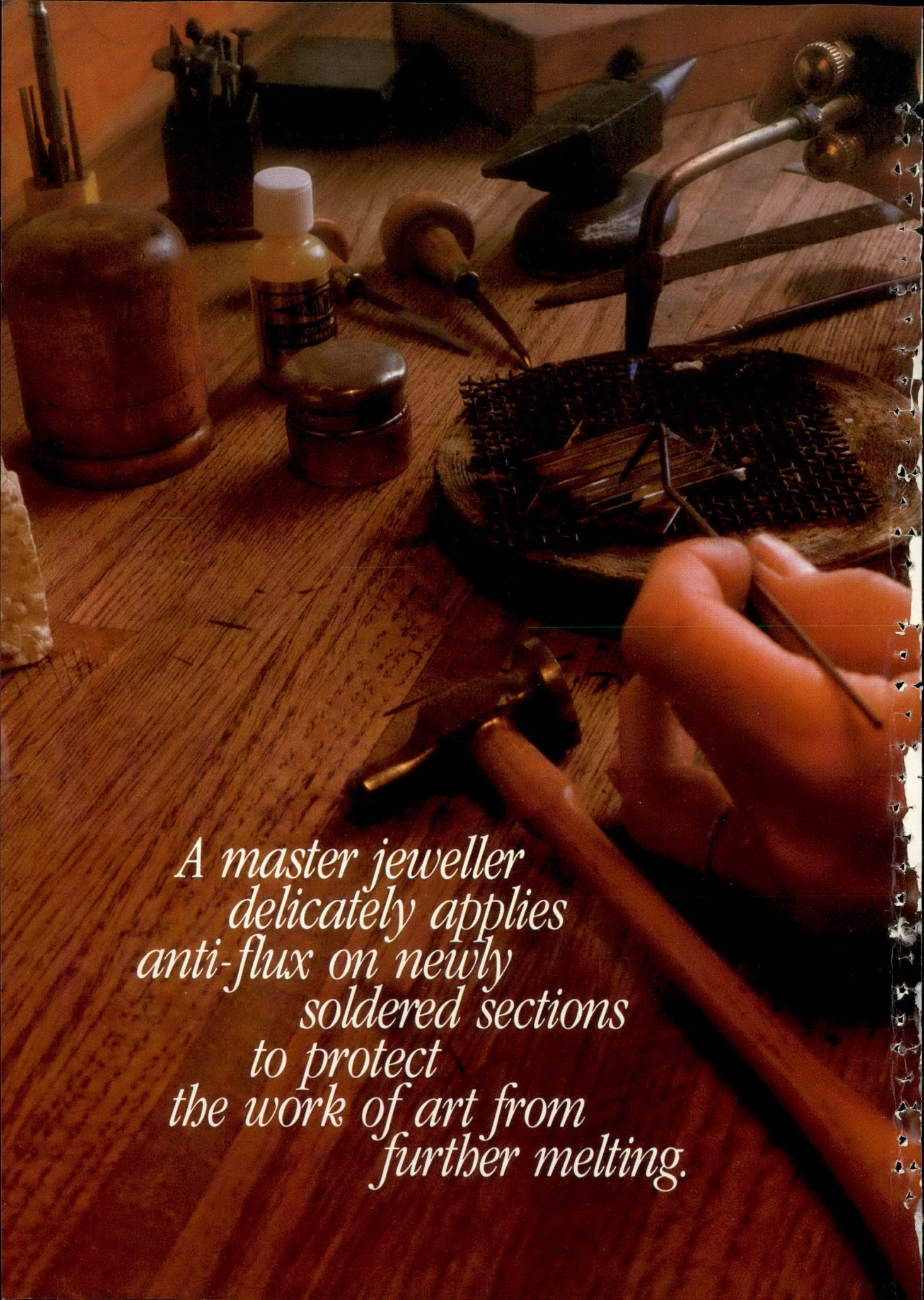

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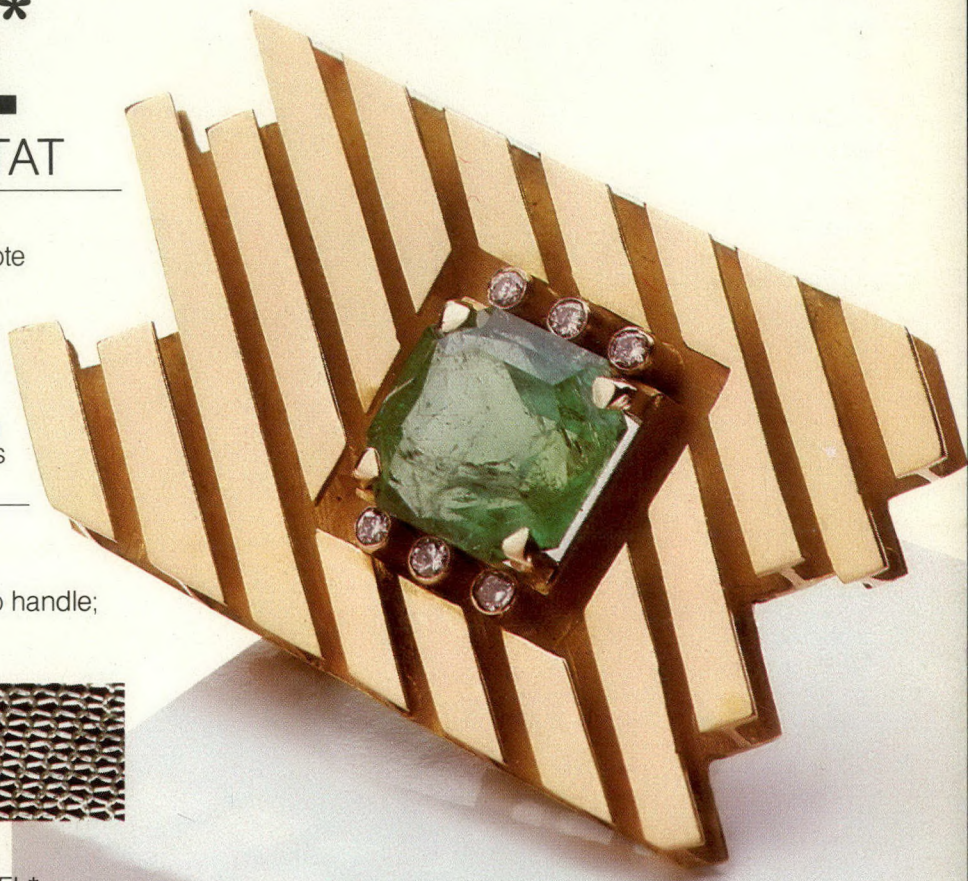

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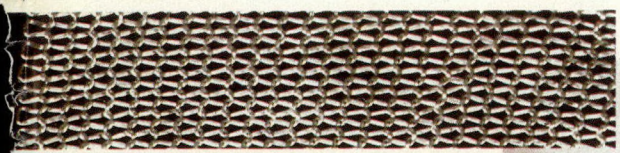

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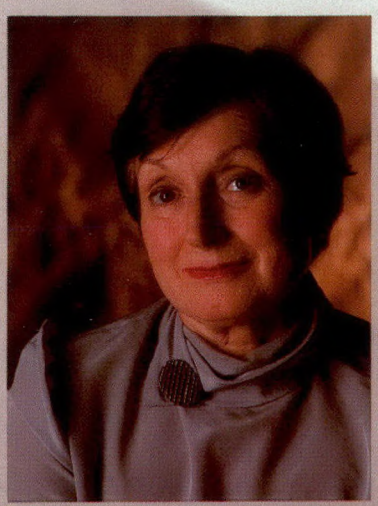

MADELEINE DANSEREAU

Ms. Dansereau is one of Canada's most renowned jewellers. She studied her craft in Canada, the United States and Italy with some of the world's finest artists. Her work has won her many awards and some are in permanent collections at the Montreal Museum of Fine Arts and at the Joan Chalmers Foundation in Toronto. She is often called upon to act as a judge at exhibitions across Canada. Presently, she is one of the co-founders of l'École de joaillerie et des métaux d'art de Montréal, where she works and teaches.

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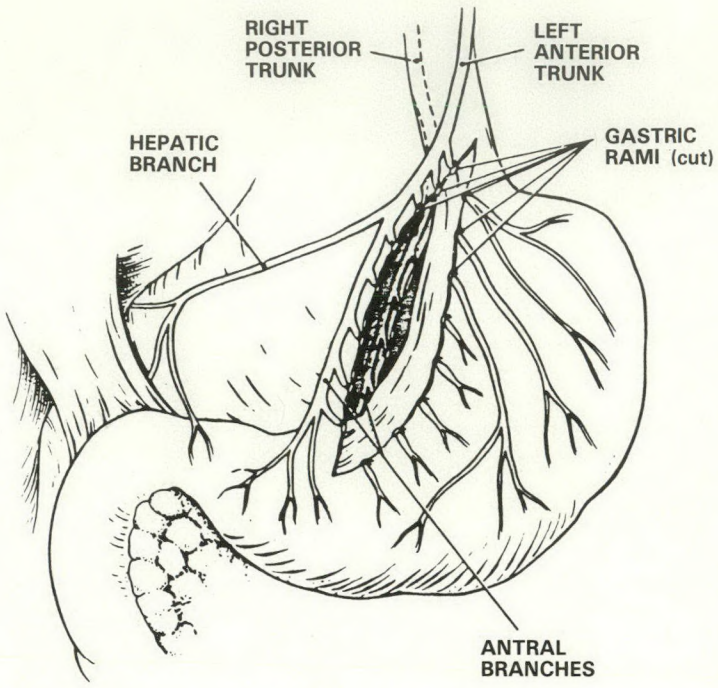

17. The procedure depicted above

(A) is frequently required for optimal results in patients with gastroesophageal reflux

(B) has no place in the management of peptic ulcer disease complicated by hemorrhage, obstruction, or perforation

(C) has been shown to be associated with substantially lower rates of recurrent peptic ulcer disease than antrectomy and truncal vagotomy

(D) diminishes the postoperative effects of destruction or bypass of the pylorus that complicate other operations for peptic ulcer

(E) is based on anatomic discoveries made during the past two decades

For the incomplete statement above select the one answer that is best of the five given. For the critique of Item 17 see page 406.

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CANADIAN ASSOCIATION OF GENERAL SURGEONS

R.F. PACE, MD;* J.V. FREI, MD, FRCP[C];† R.B. PASSI, MD, FRCS[C], FACS*

Histologic Sequelae of Endoscopic Sphincterotomy: a Canine Experiment

Concern for the late formation of strictures at the site of an endoscopic sphincterotomy has delayed the acceptance of this procedure as treatment for choledocholithiasis in otherwise healthy patients. The authors addressed this issue by comparing the biochemical and histologic sequelae of sphincterotomy in 23 dogs with those in 10 sham-operated controls.

Twenty-four hours after sphincterotomy, hemorrhagic, edematous mucosa surrounded the incision. Microscopically, there was an acute inflammatory exudate bridging the mucosal surfaces. Mucosal regeneration was sufficient after 1 week to cover the defect caused by the cautery, although some inflammatory changes were still evident.

A widely patent sphincterotomy orifice was seen in 15 dogs followed up for 10 weeks. In three dogs, the fibres of the papilla had reunited below the incision, resulting in a choledochoduodenal fistula. Histologically, complete healing of the mucosal surface had occurred with no evidence of scar formation or chronic inflammation. Serum bilirubin and liver enzyme measurements did not show evidence of biliary obstruction due to the sphincterotomy.

From the results of our study, there is no evidence to suggest that an endoscopic sphincterotomy is predisposed to late stenosis.

La crainte de voir apparaître tardivement un rétrécissement au niveau d'une sphinctérotomie endoscopique a retardé l'acceptation générale de cette intervention comme traitement de la cholédocholithiase chez des patients par ailleurs en bonne santé. Les auteurs ont abordé ce sujet par la comparaison des séquelles biochimiques et histologiques de la sphinctérotomie chez 23 chiens par rapport à 10 chiens témoins soumis à une opération simulée.

Vingt-quatre heures après la sphinctérotomie une muqueuse hémorragique et oedémateuse entoure l'incision. Au microscope on constate un exsudat inflammatoire aigu recouvrant les surfaces muqueuses. Après 1 semaine, la regénération de la muqueuse est suffisante pour couvrir les marques de cautérisation même si des changements inflammatoires sont encore évidents.

Un orifice de sphinctérotomie bien perméable a été observé chez 15 chiens qui ont été gardés sous surveillance pour jusqu'à 10 semaines. Chez trois chiens, les fibres de la grande caroncule s'étaient réunies sous l'incision entraînant la formation d'une fistule cholédocho-duodénale. À l'histologie, on observait une guérison complète de la surface muqueuse sans signe de cicatrice ou d'inflammation chronique. Le dosage de la bilirubinémie et des enzymes hépatiques n'a pas révélé de signe d'obstruction biliaire attribuable à la sphinctérotomie.

Les résultats de notre étude n'indiquent pas que la sphinctérotomie endoscopique puisse prédisposer à une sténose tardive.

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Winner of the 1983 Canadian Association of General Surgeons Residents Research Prize

Presented at the 6th annual meeting of the Canadian Association of General Surgeons, Calgary, Alta., Sept. 22, 1983

Accepted for publication Feb. 7, 1984

Reprint requests to: Dr. R.B. Passi, Department of Surgery, University Hospital, PO Box 5339, Station A, London, Ont. N6A 5A5

Endoscopic sphincterotomy is now the preferred method for treating retained or recurrent biliary calculi.[1] Although its application is unchallenged in the high-risk surgical patient, many surgeons prefer the classic operative approach to common-bile-duct calculi in otherwise healthy patients, because of concern that strictures will form later at the site of the sphincterotomy.[1-4] We attempted to resolve this issue by examining the histologic sequelae of electrosurgical sphincterotomy, using a canine model.

Material and Methods

A cholecystectomy was performed at the time of laparotomy in 33 anesthetized mongrel dogs. Through a longitudinal duodenotomy, the papilla of Vater was identified and cannulated with a sphincterotome designed for endoscopic use.

In 23 dogs (group 1), a sphincterotomy 1 to 1.5 cm long was performed by applying blended electrocautery current to the raised cutting wire. The duodenotomy and laparotomy incisions were then closed and the animals were allowed to recover. Ten control dogs (group 2) underwent cholecystectomy and duodenotomy, but a sphincterotomy was not performed.

All group 2 dogs and 15 group 1 dogs had serum bilirubin and liver enzyme levels measured daily for the first week postoperatively and thereafter at weekly intervals for 10 weeks. The remaining eight dogs in group 1 were sacrificed at varying intervals from 24 hours to 1 week postoperatively to investigate the early changes caused by the electrocautery incision.

At the time of sacrifice, the duodenotomy was reopened and the sphincterotomy orifice examined. After excision of the choledochoduodenal junction, histologic sections across the sphincterotomy were examined to ascertain the changes and the degree of healing at the incision site.

Results

The postoperative course was similar in both groups, with no complications that we could attribute to the sphincterotomy. Two dogs in group 2 died as a result of viral epidemics in the animal storage area, one 4 weeks and the other 6 weeks postoperatively.

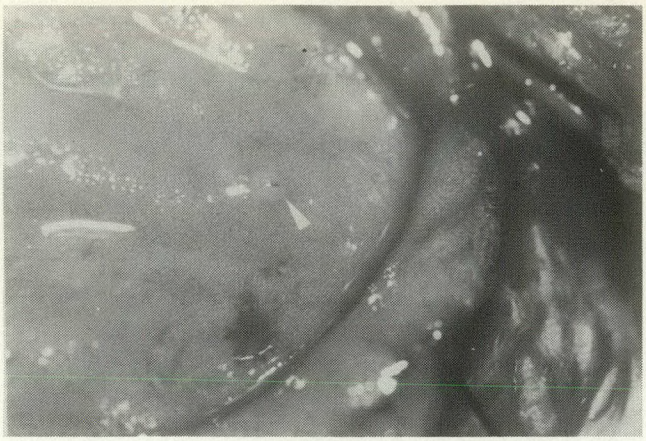

Fig. 1a

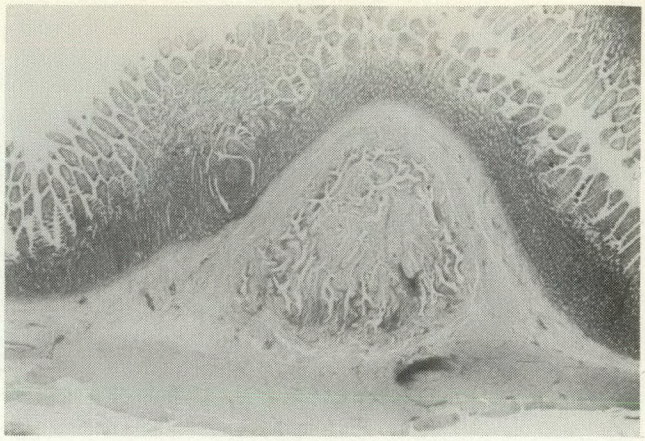

Fig. 1b

FIG. 1—(a) Duodenal papilla (arrow) in control dog. (b) Intramural portion of common bile duct. Lumen of common bile duct is filled with papillary projections of bile-duct mucosa, separated from lumen of duodenum by roof of smooth muscle and duodenal mucosa (hematoxylin-phloxine-saffron stain, reduced by 51% from × 80).

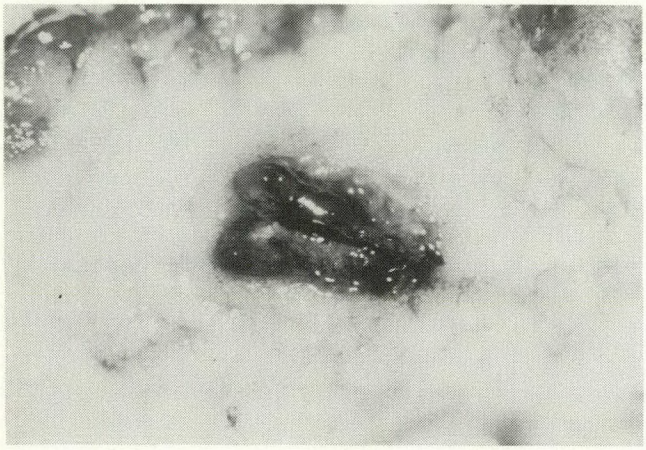

Fig. 2a

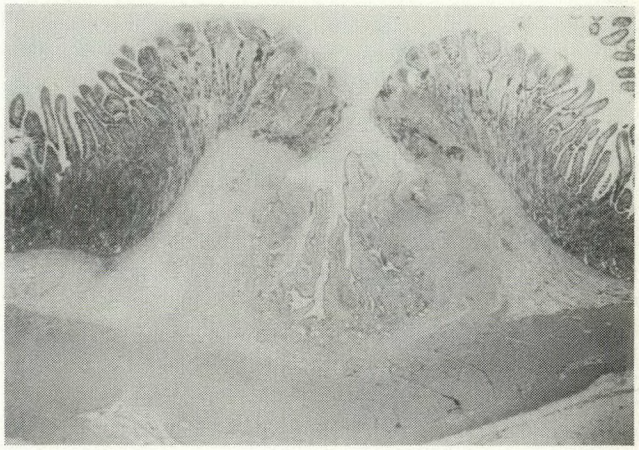

Fig. 2b

FIG. 2—(a) Sphincterotomy after 24 hours. Incision surrounded by hemorrhagic and edematous mucosa. (b) Histologic section taken across sphincterotomy after 24 hours. Acute inflammatory exudate lining incision, with hemorrhage and edema in surrounding tissue (hematoxylin-phloxine-saffron stain, reduced by 51% from × 80).

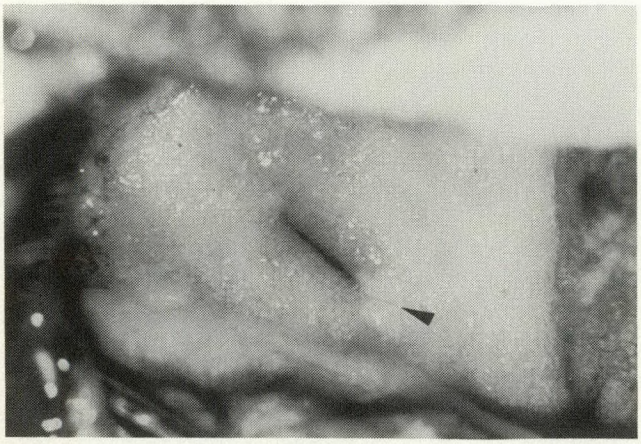

Fig. 3a

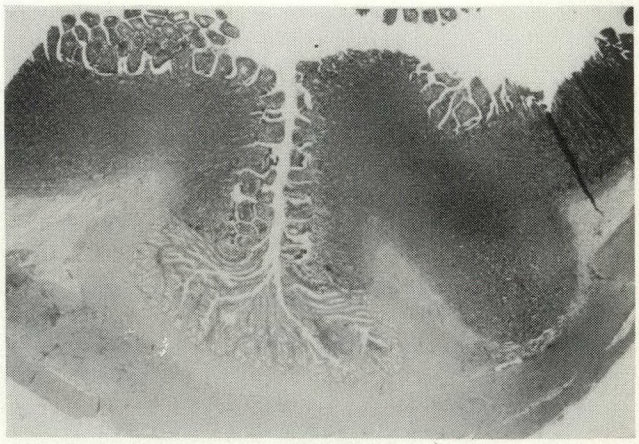

Fig. 3b

FIG. 3—(a) After 10 weeks, sphincterotomy fully healed. Divided fibres of papilla visible (arrow), with patent sphincterotomy extending proximally. (b) Histologic section shows incision lined by mature mucosal epithelium without evidence of inflammation or scar tissue at mucosal interface (hematoxylin-phloxine-saffron stain, reduced by 51% from × 80).

The serum bilirubin and liver enzyme (alkaline phosphatase, glutamic oxaloacetic transaminase and glutamic pyruvic transaminase) levels were moderately elevated after the first postoperative week, then rapidly returned to normal in both groups and remained normal for the duration of the study. No persistent or increasing biliary obstruction was evident, and there was no notable difference between the two groups.

The duodenal papilla in normal dogs (group 2) (Fig. 1a) consisted of a small mucosal elevation with a central opening for the common bile duct. From this point, the common duct ascended intramurally in the duodenal wall for a variable distance before emerging as the common bile duct proper. A microscopic section across the intramural portion of the common bile duct (Fig. 1b) showed that its lumen was filled with papillary projections of bile-duct mucosa and was separated from the duodenal lumen by a septum of smooth muscle and duodenal mucosa.

At 24 hours postsphincterotomy, gross inspection revealed hemorrhagic, edematous mucosa surrounding the sphincterotomy site (Fig. 2a). A histologic section taken across the sphincterotomy (Fig. 2b) showed the base of the incision lined by an acute inflammatory exudate, with hemorrhage and edema in the surrounding tissue. Despite this surprising degree of early local reaction, healing progressed rapidly and was nearly complete in the group 1 dogs examined at 1 week postoperatively.

At 10 weeks, all 15 dogs had a widely patent sphincterotomy orifice (Fig. 3a) with no gross signs of scarring or ongoing inflammation. In three dogs, the papillary fibres had reunited below the sphincterotomy, creating, in effect, a proximal choledochoduodenal fistula. Histologic examination of the healed sphincterotomy at 10 weeks (Fig. 3b) demonstrated a lining of mature duodenal and common-bile-duct mucosa with accurate mucosal healing in all areas. There was no evidence of scar tissue or chronic inflammatory changes at the mucosal interface or in the surrounding tissues that might predispose to late stenosis.

Discussion

Endoscopic sphincterotomy successfully clears the common bile duct in 90.5% to 93.8% of patients with choledocholithiasis, and is associated with a mortality of less than 1.5% in large series.[2,5-7] Late stenosis at the sphincterotomy site is uncommon, occurring in only 1.0% of patients followed up from 1 to 5 years.[3,5]

In early animal experiments, Kawai and associates[8] studied the feasibility of electrosurgical sphincterotomy in five dogs. They found no visible evidence of fibrosis or stenosis 2 to 4 weeks postoperatively. Tanaka and associates[9] studied three monkeys 10 to 12 months following sphincterotomy. They found that accurate mucosal healing had occurred in all cases, but failed to show convincing histologic proof of these claims. Other investigators[10] have demonstrated the safety of electrosurgical sphincterotomy in animals, but have not examined the incision to assess its potential for late scarring.

In our study, we found no evidence to suspect that an electrosurgical sphincterotomy is prone to late stenosis. The sphincterotomy remained widely patent throughout the study period, with no visual evidence of scarring or chronic inflammation. Moreover, histologic examination of the incision 10 weeks after sphincterotomy confirmed the presence of accurate mucosal healing with a remarkable absence of scar tissue formation and chronic inflammation at the mucosal interface.

Conclusions

From our study on the healing of an endoscopic sphincterotomy in a canine model, we found that within 24 hours an appreciable inflammatory response surrounded the incision. Healing progressed rapidly, however, so that after 10 weeks the incision was lined by mature mucosal epithelium without evidence of ongoing inflammation. We could find no evidence to suggest that an endoscopic sphincterotomy is predisposed to late stenosis.

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Blunt Splenic Trauma: Diagnosis and Management

To examine the morbidity and mortality associated with blunt splenic injuries, the authors reviewed the results in 106 such patients treated in the Sunnybrook Regional Trauma Unit between June 1, 1976 and June 30, 1983.

Initial assessment included peritoneal lavage in 86 patients. No patient with known or suspected splenic injury was treated nonoperatively nor were any patients found to have had splenic injuries missed at the initial assessment. Seventy-one splenectomies and 35 splenorrhaphies were performed. The overall mortality was 25% and 10 surviving patients had serious complications. The splenic injury itself was never the cause of death. Only one patient who initially underwent splenorrhaphy later required splenectomy.

It is concluded that blunt splenic injury is rarely the cause of death or serious morbidity when a policy of immediate diagnosis and operative treatment is carried out. Furthermore, in selected patients, splenorrhaphy is a safe and effective treatment.

Dans le but d'évaluer la morbidité et la mortalité rattachées aux traumatismes fermés de la rate, les auteurs passent en revue les résultats obtenus chez 106 patients victimes de telles blessures qui ont été traités au Sunnybrook Regional Trauma Unit entre le 1er juin 1976 et le 30 juin 1983.

Chez 86 patients, l'examen initial comprenait un lavage péritonéal. Aucun patient ayant un traumatisme splénique diagnostiqué ou soupçonné n'a été traité de façon non chirurgicale; de même aucun patient chez qui on a confirmé une lésion de la rate n'a échappé à l'examen initial. Soixante-et-onze splénectomies et 35 splénorraphies ont été pratiquées. Le taux de mortalité globale a été de 25% et 10 survivants ont eu des complications sérieuses. En soi, le traumatisme splénique n'a jamais été la cause du décès. Des patients qui ont subi une splénorraphie, un seul a par la suite nécessité une splénectomie.

On conclut qu'un traumatisme splénique fermé est rarement mortel ou la cause d'une morbidité sérieuse quand on recourt systématiquement à un diagnostic immédiat et à la chirurgie. De plus, chez des patients choisis, la splénorraphie s'avère un traitement sûr et efficace.

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The management of splenic injury in adults continues to be controversial. The methods of diagnosis, treatment and consequences of splenectomy have not yet been fully agreed upon. Splenic rupture can be spontaneous or caused by penetrating, blunt or operative trauma.

At the Sunnybrook Regional Trauma Unit all adult patients with splenic injury due to blunt trauma have been managed uniformly and this paper reviews the results of their management.

Patients and Methods

Only patients aged 16 years and older with splenic injuries caused by blunt trauma were included. Excluded were all patients with penetrating trauma, those initially operated upon elsewhere and transferred to Sunnybrook Medical Centre for postoperative care and all patients who died in the Emergency Department and were found at autopsy to have splenic trauma.

Of 1378 patients admitted to the Regional Trauma Unit at Sunnybrook Medical Centre between June 1, 1976 and June 30, 1983, 136 had splenic injuries. In 106 patients the splenic injury was due to blunt trauma and they were cared for entirely at Sunnybrook Medical Centre; 22 were operated upon elsewhere, 7 died before receiving definitive care and 1 suffered penetrating splenic trauma. The 106 patients are the subject of this report. There were 29 women and 77 men and they were predominantly young (Fig. 1).

When the trauma unit is notified that a patient is being transported to Sunnybrook, residents of the appropriate services are called to the trauma room in the Emergency Department. They include a trauma team leader and residents in general surgery, anesthesia, orthopedics and neurosurgery. As soon as the patient arrives, resuscitation and evaluation are carried out. Indications for operation for an intra-abdominal injury may be clear. If not, or if the abdomen cannot be evaluated because of coma, alcoholic intoxication or spinal cord injury, open peritoneal lavage is carried out in the trauma room. If the lavage fluid is grossly bloody or if its erythrocyte count is greater than 0.02×10^{12}/L (20 000/mm^3), its leukocyte count more than 0.5×10^9/L or its amylase level is more than 1750 U/L, laparotomy is done. Until Jan. 1, 1979, all splenic injuries were managed by splenectomy. Since then, splenorrhaphy has been performed if possible. Antibiotics are not given prophylactically.

An abbreviated injury severity score (1980 version) was calculated for each patient according to the rules of the American Association for Automotive Medicine.[1] This system of scoring was introduced in 1974 by the Maryland Institute for Emergency Medicine.[2] Each organ system injured is assigned a number from 1 (minor injury) to 5 (critical injury). The overall injury severity score is the sum of the squares of the individual organ system scores.

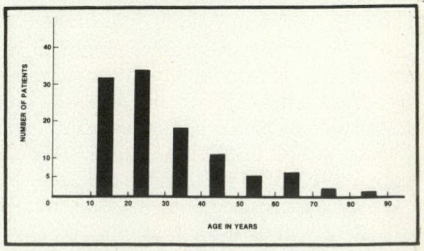

FIG. 1—Age distribution.

Statistical comparisons of injuries sustained by surviving patients and nonsurviving patients were carried out, using the χ^2 test in a 2 × 2 contingency table. Comparisons of injury severity scores were carried out with an unpaired *t*-test. Results were considered significant if p was less than 0.05.

Findings

Motor vehicle accidents accounted for 91% of the injuries in the 106 patients and the remainder were primarily due to falls. A positive result from peritoneal lavage was the main indication for laparotomy in 82% of the patients. Ten percent, however, had obvious intra-abdominal injury — usually indicated by a ruptured hemidiaphragm on chest roentgenogram. The others underwent surgery on the basis of a clinical diagnosis of intra-abdominal injury. In 102 of the 106 patients, other injuries were present (Tables I and II). Surviving patients had an average of 2.3 while nonsurviving patients had an average of 2.9 other organ systems injured (Fig. 2). The severe nature of these injuries is reflected in the distribution of injury severity scores (Figs. 3 and 4).

All patients with evidence of, or with a possibility of, intra-abdominal injury were operated upon immediately. No patient with negative findings on peritoneal lavage or thought clinically to have no intra-abdominal injury had signs or symptoms suggestive of splenic injury subsequently. Seventy-one patients underwent splenectomy and 35 splenorrhaphy (Table III).

No splenorrhaphies were performed before Jan. 1, 1979. Since then, this form of management has become increasingly popular (Fig. 5). Complications of the injuries and their management have been surprisingly few. In 10 patients (13% of survivors) there were 12 complications. These included subphrenic abscess, pancreatic injury, pulmonary embolism and upper gastrointestinal bleeding. All but one had had a splenectomy. The mean (± SEM) injury severity score for those patients who had complications was 38.6 ± 11.0. Seventy-nine of the 106 patients survived their injuries and were discharged from hospital. The mean injury severity score of the 79 survivors was 34.5 ± 11.3 and of the 27 nonsurvivors 52.4 ± 10.4 (Table IV and Fig. 4). The mean injury severity score of all survivors was significantly ($p < 0.005$) different from the score of those who died. Fifteen (56%) of the 27 nonsurvivors died of closed head injuries, 7 (26%) died of uncontrollable hemorrhage from severe hepatic injuries and retroperitoneal bleeding, 4 (15%) survived their prolonged hypovolemic shock only to succumb to multiple organ system failure. One patient with multiple fractures and a flail chest died of pulmonary embolism.

Discussion

The diagnosis and management of

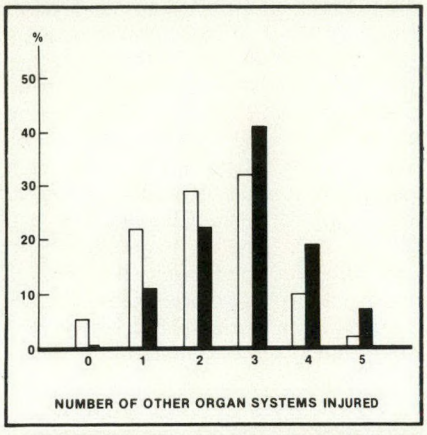

FIG. 2—Number of organ systems injured other than gastrointestinal tract. White bars = survivors, black bars = nonsurvivors.

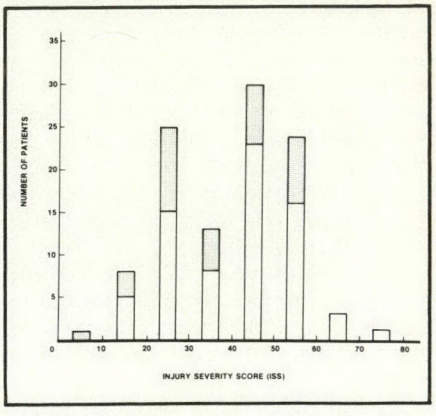

FIG. 3—Splenectomy (white bars) or splenorrhaphy (shaded bars) and injury severity score.

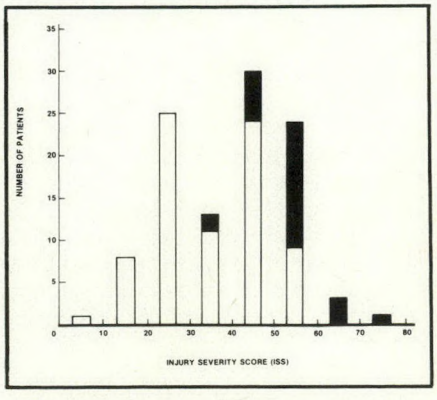

FIG. 4—Survivors (white bars), nonsurvivors (black bars) and injury severity score.

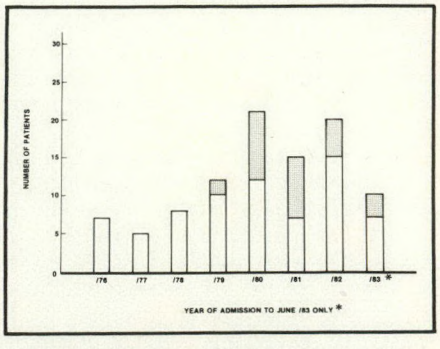

FIG. 5—Splenectomy (white bars), splenorrhaphy (shaded bars) and date of admission.

Table III—Operative Management

Procedure	No. (%)
Splenectomy	71 (67)
Partial splenectomy	0
Splenic suture	8 (8)
Hemostatic agent	22 (21)
None	5 (5)

Table I—Associated Injuries

Injury	Survivors, no. (%) (n = 79)		Nonsurvivors, no. (%) (n = 27)
Central nervous system or spinal cord	33 (42)	*	20 (74)
Face	18 (23)	*	3 (11)
Blunt chest	38 (48)		15 (56)
Other intra-abdominal	32 (41)	*	20 (74)
Genitourinary	14 (18)		6 (22)
Multiple systems	49 (62)		17 (63)

*Difference significant as determined by χ^2 test at the 5% level.

Table II—Intra-abdominal Injuries Associated with Splenic Trauma

Injury	Survivors, no. (%) (n = 79)	Nonsurvivors, no. (%) (n = 27)
Ruptured diaphragm	6 (8)	6 (22)
Liver	22 (28)	14 (52)
Hollow viscus (including serosal tears)	14 (18)	4 (15)
Retroperitoneal (excluding genitourinary)	16 (20)	9 (33)

blunt splenic injury has undergone a marked change in the last 10 years. Diagnosis made on the basis of physical examination and clinical suggestion is difficult in patients with multiple injuries. Peritoneal lavage, when carried out through a mini-laparotomy incision, is a safe and rapid method of detecting the presence of intra-abdominal blood in the patient who has received blunt trauma. False-negative results are extremely rare and false-positive findings can be avoided by careful insertion of the catheter.[3] Peritoneal lavage provides a rapid method of determining the necessity for laparotomy while the patient is still in the emergency department and eliminates the need for time-consuming radiologic or nuclear medical tests. We believe that the policy of observation of adult patients with possible splenic injuries is to be condemned. To wait for generalized peritonitis or hypotension secondary to hypovolemia to develop is to invite complications.

Although the diagnosis of blunt splenic injury has been greatly simplified and expedited in the last 10 years, its management has become more complex. Two factors account for this complexity. First, the Hospital for Sick Children in Toronto has amply demonstrated the efficacy of conservative management of splenic injuries in children.[4] This has occasionally been tried in adults, but no results have been published. Over 90% of the patients in this series had injuries to other organs, many of which required one or more operative procedures. In particular, 41% of our surviving patients and 74% of those who died had other intra-abdominal injuries. In this group it would be difficult to select those with splenic injury as their only intra-abdominal injury. Furthermore, it would be hazardous to subject even patients with isolated splenic injury to prolonged anesthesia for orthopedic procedures, as it would be difficult to determine the cause of any hypotensive episodes. Thus, we believe that it is simpler and safer to treat all splenic injuries by immediate operation.

The second factor that has increased the complexity of treatment is the suggestion that splenectomy can have adverse effects on host-defence mechanisms. Total splenectomy in childhood has definitely been shown to result in an increased incidence of overwhelming septicemia leading to rapid death.[5] In adults, however, it has been very difficult to prove that overwhelming postsplenectomy sepsis even exists. One study in adults suggested an incidence of postsplenectomy sepsis of 2.2% in 45 months of follow-up of healthy adult patients who underwent splenectomy for a variety of reasons.[6] A matched group of patients who underwent other operations had no deaths due to sepsis in this period. Although this study suffers from the usual problems of a retrospective chart review, it does appear to indicate a small but definite risk associated with asplenia in the adult. The pathophysiology of this state has recently been reviewed.[5] This has led to numerous attempts to salvage splenic tissue. Suggested methods have ranged from a nonoperative approach (already condemned) to operative salvage of the spleen to implantation of splenic tissue into the peritoneal cavity[7] or portal vein.[8] The only form of splenic conservation we have experience with is a direct attack on the bleeding site. This includes partial splenectomy,[9] splenic suture, splenic artery ligation,[10] the application of a hemostatic agent and no treatment (Table III). In our series, no partial splenectomies or splenic artery ligations were carried out. It is our belief that if the spleen has been so damaged that only a partial splenectomy can salvage a portion of it, it is better to proceed with total splenectomy to save time and reduce blood loss in these multiply injured patients. The splenic vessels pass out radially from the hilum of the spleen, dividing the spleen into several poorly defined segments.[11] This anatomical arrangement makes partial splenectomy technically possible. It also allows the spleen to be sutured by passing the sutures at right angles to the vessels. Of our 35 patients who underwent splenorrhaphy, 8 required sutures to control bleeding. However, we have not had success in attempting to suture disrupted hilar vessels. Patients with this injury should undergo a total splenectomy. Most patients (22 of 35) required simply the application of hemostatic agents (e.g., Avitene, Oxycel) and laparotomy sponges to the bleeding site to obtain hemostasis. Usually 5 to 10 minutes of such packing is all that is required. Five patients had small capsular tears which had stopped bleeding by the time the spleen could be observed at laparotomy. It is interesting that whereas most splenic injuries in childhood will stop bleeding spontaneously, in our adult series, at least 30 of 35 did not.

Special mention should be made of one patient. At the time of operation, this patient was in severe hypovolemic shock due to multiple injuries resulting from an automobile accident. The splenic injury was repaired with hemostatic materials and sutured and other injuries were attended to. Twelve hours later, the patient was operated upon again because of continued intra-abdominal bleeding. At laparotomy, there was a blood clot about the spleen, and a previously repaired bladder injury was actively bleeding. The spleen was removed and the bladder repaired a second time. However, the patient died later the same day from irreversible hypovolemic shock. This case illustrates the principle that hemodynamically unstable patients who require large quantities of blood with the subsequent, almost inevitable, coagulopathy are not candidates for splenic repair.

A retrospective chart review is a poor method of determining complication rates. Only complications noted in the chart are tabulated. Nevertheless, it is clear that the complication rate associated with the operative management of splenic injuries is reasonably low. Only 13% of our surviving patients had complications that could possibly be attributed to the splenic injury. All but one had undergone total splenectomy. Two pancreatic fistulas were noted, at least one of which was likely an iatrogenic injury. Six patients had sepsis — one had a wound infection, four had intra-abdominal abscesses and one had severe pneumonia. Patients who had abscesses had other intra-abdominal injuries — usually liver lacerations or bowel perforations — that

Table IV—Mean Injury Severity Scores

Group	No. of patients	Score, mean ± SEM
All survivors	79	34.5 ± 11.3
Survivors with complications	10	38.6 ± 11.0
Survivors without complications	68	33.8 ± 11.1
Survivors with splenectomy	50	35.8 ± 11.4
Survivors with splenorrhaphy	28	32.1 ± 11.0
Nonsurvivors	27	52.4 ± 10.4

Table V—Morbidity and Mortality in Patients Who Underwent Splenectomy and Splenorrhaphy

Group	Splenectomy (n = 71)	Splenorrhaphy (n = 35)
Survivors	50	29
Survivors with complications	9	1

clearly contributed to the onset of sepsis. Four patients had miscellaneous complications — jaundice, pulmonary embolism and stress upper gastrointestinal bleeding — that were at least partially a result of the splenic injury and its treatment. Most noteworthy is that the 35 patients who underwent splenorrhaphy had only one complication associated with this treatment (stress gastrointestinal bleeding). On the other hand, patients treated by splenorrhaphy had less severe injuries than those who required splenectomy, although the difference in injury severity score was not substantial.

Of the 106 patients operated upon at Sunnybrook Medical Centre, 27 died — a mortality of 25%. This contrasts with a mortality of 18.6% in a large series of patients at the University of Texas.[12] Our slightly higher mortality likely reflects the fact that 85% of our trauma patients are referred from other centres and hence tend to have more serious injuries. As might be expected, most of our patients who died had severe head injuries (56%). Uncontrollable hemorrhage and prolonged shock accounted for only 11 deaths. In the large Texas series, shock was the commonest cause of death. Again, we believe that the difference is due to the contrasting patient populations. Our mortality could only be improved by the more rapid transportation of critically injured patients to well-equipped and well-staffed emergency departments.

In Table V, we compare morbidity and mortality of patients who underwent splenectomy or splenorrhaphy. However, as noted above, this does not indicate that splenorrhaphy is a safer operation than splenectomy; rather, patients treated by splenorrhaphy tended to be less severely injured than those treated by splenectomy.

Conclusions

Splenic injuries due to blunt trauma can now be diagnosed and treated in a prompt and straightforward fashion. Splenorrhaphy is a safe and effective form of treatment in the stable patient with an easily repairable splenic injury.

Our thanks to Miss Lilli Boctor for assisting in the chart review and Miss Malca Kates for typing the manuscript.

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Value of High-Resolution Computerized Tomography in Localizing Diseased Parathyroid Glands

Eighteen patients with hyperparathyroidism underwent high-resolution computerized tomography of the neck and superior mediastinum to assess the accuracy of the method in localizing diseased parathyroid glands preoperatively. The tomograms were correlated with surgical and pathological findings. Four scans were technically unsatisfactory. Of the remaining 14 scans, 8 showed an enlarged parathyroid gland; in 7 cases, the scan correctly identified the location of the diseased gland while in 1 case, the side of the lesion was incorrect. The other six scans did not show an abnormal parathyroid. These glands varied in size from 0.05 to 5.0 cm^3 at the time of pathological examination. Three patients were undergoing re-exploration for persistent disease; technically acceptable scans were obtained in two and, in both, the location of the adenoma was correctly identified. Excluding patients with technically unsatisfactory scans, this technique has a sensitivity of 50% (7/14) and a false-negative rate of 43% (6/14) independent of gland size. However, in the eight scans interpreted as positive, the correct side of the lesion was localized in 7 (88%).

This technique is not recommended for routine preoperative localization but may be of value in re-exploration for persistent disease.

Dix-huit patients souffrant d'hyperparathyroïdie ont subi une tomodensitométrie à haute résolution du cou et du médiastin supérieur afin d'évaluer la précision de cette méthode quand il s'agit de localiser des parathyroïdes pathologiques en préopératoire. Les tomogrammes ont été mis en parallèle avec les constatations chirurgicales et les résultats de pathologie. Quatre scintigraphies étaient techniquement insatisfaisantes. Sur les 14 autres tomographies, 8 révélaient des parathyroïdes hypertrophiées; dans 7 cas, la scintigraphie identifiait correctement la localisation de la glande malade alors que dans le dernier cas, le côté de la lésion était erronée. Les six autres tomographies n'ont révélé aucune parathyroïde anormale. La taille de ces glandes variait de 0.05 à 5.0 cm^3 au moment de l'examen pathologique. Trois patients subissaient une seconde intervention exploratoire pour la persistance de la maladie; une tomographie techniquement acceptable a été obtenue dans deux cas permettant les deux fois de localiser correctement l'adénome. Si l'on exclut les patients dont la scintigraphie a été techniquement insatisfaisante, la sensibilité de la technique a été de 50% (7/14) et le taux de faux négatifs de 43% (6/14), indépendamment de la taille de la glande. Toutefois, sur les huit tomographies positives, le côté pathologique a été localisé correctement 7 fois (88%).

Cette technique n'est pas recommandée comme moyen systématique de localisation préopératoire. Elle peut toutefois être utile lorsqu'il s'agit de réévaluer une maladie persistante.

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Once considered rare, primary hyperparathyroidism is now being diagnosed more frequently and at an earlier stage. The widespread availability of the multichannel autoanalyser for routine determination of serum calcium concentration and highly sensitive assays for parathyroid hormone facilitate diagnosis and treatment. Surgery for primary hyperparathyroidism, especially when performed infrequently, can be difficult because the parathyroid glands are small and their location is variable. Numerous preoperative localization techniques have been tried in an effort to aid the surgeon at the time of exploration.

The purpose of this study was to assess the accuracy and value of computerized tomography of the neck and mediastinum, using a high-resolution technique, for preoperative localization of diseased parathyroid glands.

Materials and Methods

Eight men and 10 women (age range from 19 to 75 years, mean 55 years) with hyperparathyroidism were studied in a consecutive, prospective manner. The diagnosis was primary hyperparathyroidism in 17 patients and tertiary hyperparathyroidism in 1 patient. Fifteen patients underwent primary neck exploration and 3 patients had reoperation for persistent disease following neck exploration elsewhere. All had abnormally elevated serum calcium and plasma parathormone levels preoperatively.

Our surgical technique and philosophy have been described in detail previously.[1] Both sides of the neck are carefully explored and an attempt is made to identify all parathyroid glands. All normal-appearing glands are biopsied for histologic confirmation and all grossly abnormal-appearing glands are excised.

Computerized tomography was performed immediately preoperatively at the Montreal Neurological Institute by a high-resolution technique used to investigate carotid and cerebral abnormalities. This technique employs high voltage (140 kV) and a high-resolution comb that produces an enlarged image. The patients were scanned from the hyoid bone to the superior mediastinum every 13 mm. Scan interpretations were based upon a final retrospective, but blinded, reading by a skilled tomographer. All findings were correlated with the intraoperative findings and the final pathological description of the gland, including gross size, weight and histologic findings.

Results

In four patients the scans were unsatisfactory for interpretation; in three the

presence of surgical clips created artefacts and in one the scan was technically poor. In the remaining 14 patients, an abnormality was identified in eight scans, but no abnormality was seen in six.

In the eight patients whose scan showed an abnormality, the scanning technique correctly identified the location of the diseased gland in seven. All of these patients had single adenomas, which were more than twice normal gland size (Figs. 1 and 2). In the one patient in whom tomography incorrectly identified a diseased gland, the scan unequivocally suggested a right-sided lesion instead of the left-sided adenoma found at operation.

In six patients, the scan failed to identify any enlarged abnormal parathyroid tissue. Of these, four patients had single adenomas while two had multigland hyperplasia (Fig. 3).

Three patients underwent reoperation for persistent hypercalcemia following neck exploration at other institutions. All were found to have parathyroid adenomas in the superior mediastinum. In one the scan was technically unacceptable. In the two others the lesion was correctly identified by computerized tomography (Fig. 4).

In patients whose scan was positive, the glands ranged in size from 0.1 to 3.0 cm^3. In the six patients with a negative scan, the abnormal parathyroid glands were of similar size, ranging from normal to grossly enlarged (Table I).

Discussion

Many techniques have been described for preoperative identification and localization of diseased parathyroid glands. Radionuclide scanning with selenomethionine has been advocated.[2] This modality has not become popular because the false-positive rate is greater than 50%. Cine-esophagography has a reported accuracy of only 25%[3] and is reliably positive only if the abnormal gland is located adjacent to the esophagus and is associated with markedly elevated levels of serum calcium and plasma parathyroid hormone. Thyroid lymphography, originally described by Kato and associates,[4] has been reported to be highly accurate but only in a small series of four patients. Thermography, with an accuracy of less than 40%,[5] cannot detect mediastinal glands or identify the exact number of diseased glands. Arteriography provides accurate localization in 50% to 77% of cases.[6,7] However, this technique carries serious risks of arterial occlusion and neurologic sequelae.

Venous catheterization with serial sampling for parathyroid hormone levels can be sensitive and accurate in experienced hands. Arteriography with demonstration of the venous phase should be carried out before the venous sampling for accurate localization and interpretation.[8] The patients are therefore subjected to the described risks of arteriography as well. The combined procedure has an accuracy of greater than 90% in some series but requires considerable time

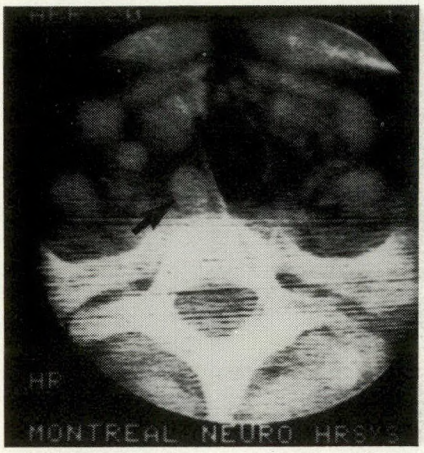

FIG. 1—Computerized tomogram of neck in 53-year-old man with primary hyperparathyroidism demonstrates large, well-defined, rounded mass (arrow) 1.5 cm in diameter to left of esophagus, indenting left posterolateral wall of trachea at T1.

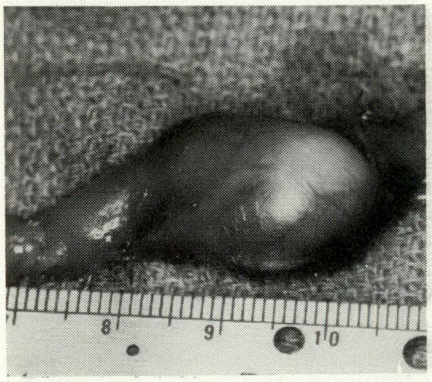

FIG. 2—Same patient as in Fig. 1. Large adenoma was found in superior pole of left lobe of thymus at operation.

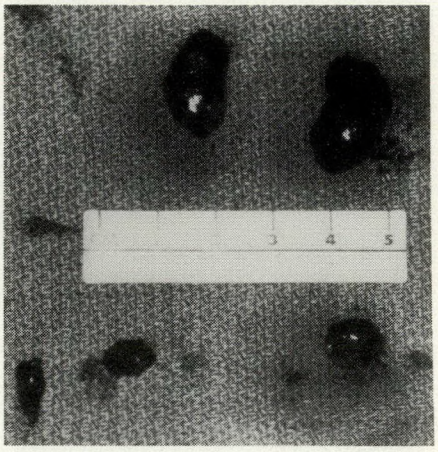

FIG. 3—Five hyperplastic glands found at operation on 60-year-old woman with primary hyperparathyroidism. Computerized tomogram had failed to demonstrate any abnormality despite several grossly enlarged glands.

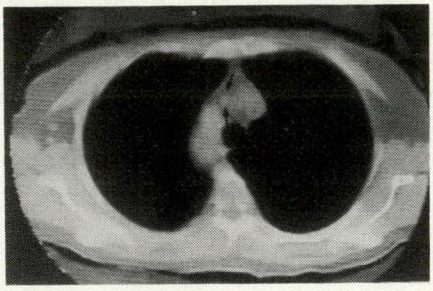

FIG. 4—Computerized tomogram of mediastinum in 53-year-old woman with persistent primary hyperparathyroidism following neck exploration reveals lesion above arch of aorta, 2 cm anterior to trachea. Parathyroid adenoma was identified at operation at this location.

Table I—Patient Data

Scan	Patient no.	Diagnosis	Gland volume, cm^3
Positive (n = 8)	1	A	0.1
	2	A	0.5
	3	A	1.2
	4	A	1.3
	5	A	1.5
	6	A	2.0
	7	A	3.0
	8	A	3.0
Negative (n = 6)	9	H	—
	10	H	0.05–0.13
	11	A	1.5
	12	A	1.5
	13	A	1.8
	14	A	5.0
Unsatisfactory	15	A	0.6
(n = 4)	16	A	1.0
	17	A	3.0
	18	A	—

A = single adenoma, H = hyperplasia.

and expertise. It is generally reserved for complicated cases when the patient must undergo re-exploration. Ultrasonography, using sensitive, small probes, has an accuracy of greater than 70% when the glands are more than 1 cm in diameter or weigh more than 1 g.[9]

In the present study, 18 consecutive patients underwent preoperative computerized tomography of the neck and mediastinum using a sensitive high-resolution technique. In four (22%) patients, the scans were unacceptable. In the remaining 14, scanning resulted in correct localization of the site of diseased glands in 7 for a true-positive ratio or sensitivity of 50% (7 of 14). There was a false-positive result in 7% (1 of 14). The false-negative rate was 43% (6 of 14). Despite the poor sensitivity and a high rate of negative scans associated with this technique, it is noteworthy that when an abnormality was detected (eight patients) it was correct in 88% (seven). Moreover, when the abnormal parathyroid gland was located in the mediastinum (three patients), the high-resolution technique correctly localized the abnormality in both patients in whom an acceptable scan was obtained. The low density of mediastinal fat may render enlarged parathyroid glands more visible in this location. Similar results have been reported in a small series by Doppman and colleagues.[10]

Many factors may be responsible for the high number of negative neck scans. As can be seen in Table I, both greatly and minimally enlarged glands were missed. Therefore, size alone is not critical for detection by this technique. The slice thickness of 13 mm may play a role. The close proximity of a major artery and veins with their branches viewed in cross-section and the proximity to the thyroid gland with similar density and frequent irregular outline may present further difficulties.

In patients with hyperparathyroidism, surgery is successful in over 90% of cases if performed by a competent, experienced surgeon. Invasive, costly and potentially hazardous procedures are not required preoperatively. All noninvasive procedures described to date have poor sensitivity, including computerized tomography, despite the use of a high-resolution technique as described here. Computerized tomography of the neck and mediastinum therefore appears to be of limited value for routine preoperative localization of diseased parathyroid glands. The need for reader expertise, the high cost and exposure to radiation are all factors to be considered, in addition to the low yield independent of gland size. However, this technique may be valuable in those patients who undergo re-exploration for persistent disease, particularly if it is located in the mediastinum.

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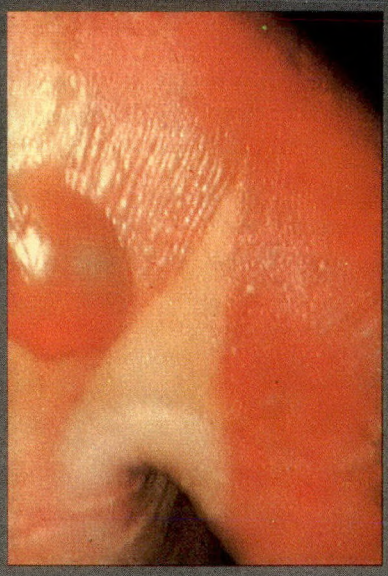

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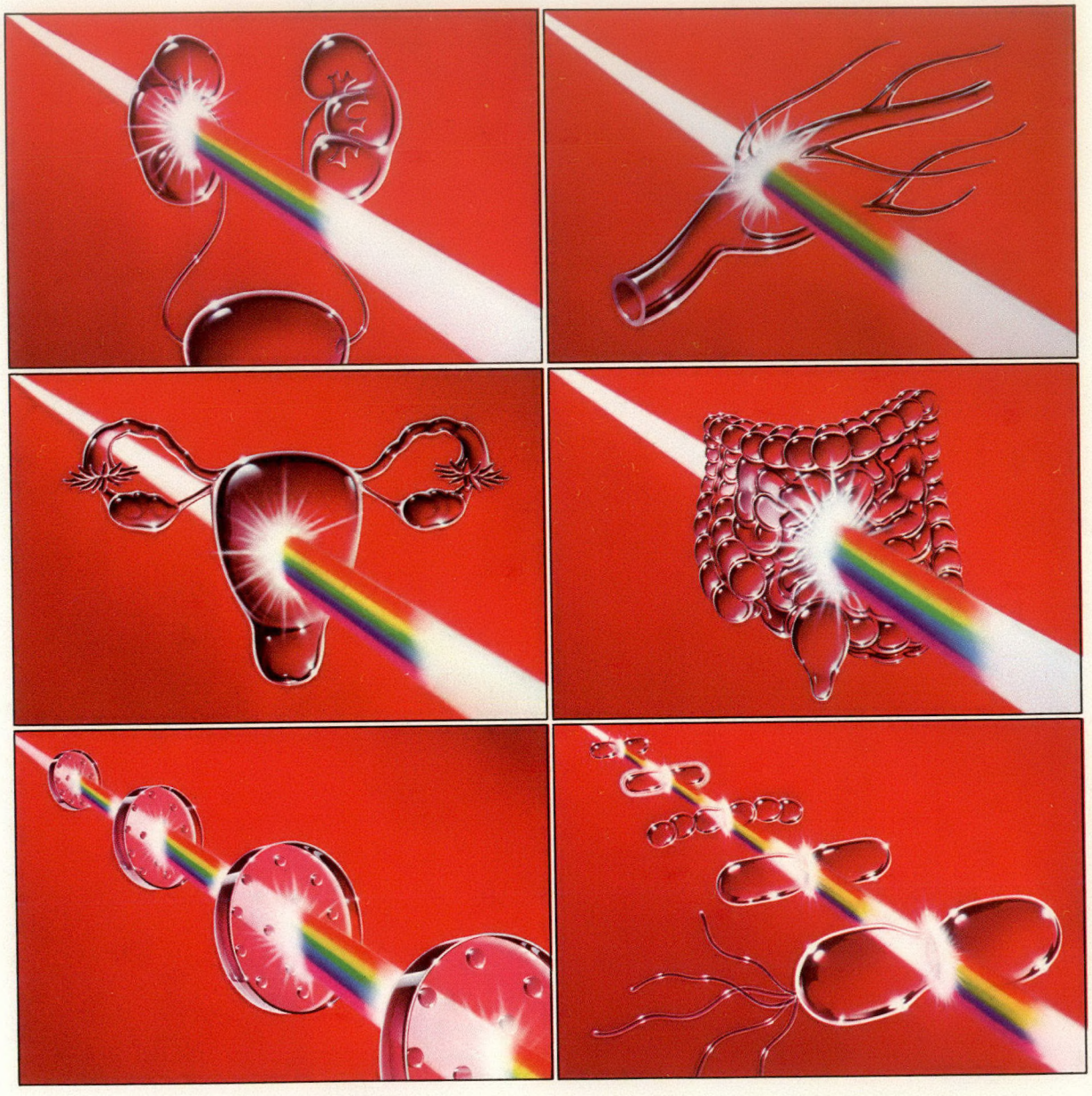

Pipracil is an effective advanced agent for gram negative, gram positive and anaerobic infections.

Pipracil (piperacillin sodium) is a major advance in presumptive antibiotic therapy. The bactericidal spectrum of Pipracil is broader than other antibiotics, such as the aminoglycosides, cephalosporins, penicillins and clindamycin. Yet Pipracil has an excellent clinical safety profile, with a low sodium content and with no reported nephrotoxicity, ototoxicity or pseudomembranous colitis. In addition, Pipracil achieves excellent concentrations in body tissues and fluids. By providing a high degree of efficacy in a wide range of mixed infections, Pipracil is a logical therapeutic alternative for presumptive therapy in surgery, urology and gynecology, including patients with impaired host defences.

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PIPRACIL*

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ter-Antibiotic for Intravenous and Intramuscular Use

ATIONS AND CLINICAL USES: Treatment of serious infections caused by susceptible strains of the designated isms in the conditions listed below.

ra-Abdominal Infections including hepatobiliary and surgical infections caused by Escherichia coli, Pseudo- s aeruginosa, enterococci. Clostridium sp., anaerobic cocci, and Bacteroides sp., including B. fragilis.

Urinary Tract Infections (complicated and uncomplicated) caused by Escherichia coli, Klebsiella sp., Pseudomonas ginosa, Proteus mirabilis and enterococci. Also uncomplicated urethritis caused by Neisseria gonorrhoeae.

Gynecological Infections including endometritis and pelvic inflammatory disease caused by Bacteroides sp., ding B. fragilis, anaerobic cocci, Neisseria gonorrhoeae, and enterococci (Streptococcus faecalis).

Septicemia caused by Escherichia coli, Klebsiella sp., Serratia sp., Proteus mirabilis, S. pneumoniae, enterococci, domonas aeruginosa, Bacteroides sp., and anaerobic cocci.

Lower Respiratory Tract Infections caused by Escherichia coli, Klebsiella sp., Enterobacter sp., Pseudomonas ginosa, Serratia sp., Haemophilus influenzae, Bacteroides species and anaerobic cocci. Although improvement een noted in patients with cystic fibrosis, lasting bacterial eradication may not be achieved.

Skin and Skin Structure Infections caused by Escherichia coli, Klebsiella sp., Serratia sp., Acinetobacter sp., obacter sp., Pseudomonas aeruginosa, indole-positive Proteus sp., Proteus mirabilis, Bacteroides sp., including gilis, anaerobic cocci and enterococci.

Bone and Joint Infections caused by Pseudomonas aeruginosa, enterococci, Bacteroides sp., and anaerobic cocci.

PIPRACIL* is useful for the treatment of mixed infections and presumptive therapy prior to the identification causative organisms; infections produced by organisms resistant to other penicillins, some aminoglycosides ephalosporins; and infections at various sites caused by streptococcus species including Group A beta-hemo- Streptococcus and Streptococcus pneumoniae.

PIPRACIL* may be administered as single drug therapy in some situations where normally two antibiotics t be employed. In vitro synergism has been shown between Piperacillin and some aminoglycosides in some erial strains. PIPRACIL* has been used clinically with aminoglycosides, especially in patients with impaired host nces. Both drugs were used in full therapeutic doses.

PIPRACIL* can be used safely in combination with a penicillinase-resistant penicillin, e.g. oxacillin, in mixed tions when beta-lactamase-positive Staphyloccus aureus is isolated along with piperacillin-susceptible nisms. It may be administered concomitantly with a cephalosporin, provided that an additive or synergistic acterial action of the two antibiotics is ascertained through in vitro tests. Based on in vitro data, cefoxitin should e given with piperacillin when Pseudomonas infections are suspected or confirmed.

Because PIPRACIL* is excreted not only renally, but also by the biliary route, it can be used in patients with tobiliary infections, or severely restricted kidney function, and in patients who have had nephrotoxic reactions her drugs, with appropriate adjustment of dosage (See DOSAGE).

Appropriate cultures should be made for susceptibility testing before initiating therapy and therapy adjusted, propriate, once the results are known.

RAINDICATIONS: A history of allergic reactions to any of the penicillins and/or cephalosporins.

RNINGS: Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients ving therapy with pencillins. These reactions are more apt to occur in persons with a history of sensitivity to iple allergens.

Cross-sensitivity of patients to penicillins and cephalosporins has been reported. Before initiating therapy with ACIL,* careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalospo- and other allergens.

If an allergic reaction occurs, the antibiotic should be discontinued.

SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE. GEN, INTRAVENOUS STEROIDS, AIRWAY MANAGEMENT, INCLUDING INTUBATION, SHOULD ALSO BE ADMINIS- ED AS NECESSARY.

AUTIONS: Bleeding manifestations have occurred in some patients receiving beta-lactam antibiotics including acillin. These reactions have sometimes been associated with abnormalities of coagulation tests such as ng time, platelet aggregation and prothrombin time and are more likely to occur in patients with renal failure. f bleeding manifestations or significant leukopenia occur, PIPRACIL* should be discontinued and appropriate apy instituted.

The possibility of the emergence of resistant organisms and the development of superinfections should be in mind, particularly during prolonged treatment.

As with other penicillins, patients may experience neuromuscular excitability or convulsions if higher than mmended doses are given intravenously.

Dosage adjustment should be made in renal insufficiency.

PIPRACIL* is a monosodium compound containing 1.98 milliequivalents (45.5 mg) of Na+per gram based on content which includes the U.S.P. allowed average. The calculated value, based on molecular weight is 1.85 Vg (42.55 mg.). Periodic electrolyte determinations should be made in patients with low potassium reserves the possibility of hypokalemia should be kept in mind with patients who have potentially low potassium ves, receiving cytotoxic therapy or diuretics. Electrolyte and cardiac status should also be monitored during nged-treatment in patients with impaired cardiac function.

Prior to treatment, patients with gonorrhea should also be evaluated for syphilis. Specimens for darkfield ination should be obtained from patients with any suspected primary lesions, and serologic tests should be rmed. In all cases where concomitant syphilis is suspected, monthly serological tests should be made for a mum of 4 months.

The use of some penicillins (ampicillin, amoxicillin) has been associated with morbilliform rashes in some s of infectious mononucleosis. PIPRACIL* should be used with caution in the treatment of patients with infec- s mononucleosis.

Interactions: The mixing of PIPRACIL* with an aminoglycoside in vitro can result in substantial inactivation of the noglycosides.

e During Pregancy or Lactation: Safety of PIPRACIL* use in pregnant women has not been determined. Because nal reproduction studies are not always predictive of human response, this drug should be used during pregnancy if clearly needed. It has been found to cross the placenta in rats. Caution should be exercised when PIPRACIL* dministered to nursing mothers. It is excreted in low concentrations in milk.

atric Use: Dosages for children under the age of 12 have not been established.

ERSE REACTIONS: PIPRACIL* is generally well tolerated. The most common adverse reactions have been local in ure, following intravenous or intramuscular injection. The following adverse reactions may occur:

Local Reactions – In clinical trials thrombophlebitis was noted in 3.8% of patients. Pain, erythema, and/or indura- at the injection site in 1.9% of patients. Less frequent reactions: ecchymosis, deep vein thrombosis and matomas.

Hypersensitivity Reactions – Rash was noted in 1.9% of patients. Drug fever 2.1%. Less frequent findings: pruritis, cular eruptions, positive Coombs tests.

Gastrointestinal – Diarrhea and loose stools were noted in 2.8% of patients. Less frequent reactions: vomiting, ea, bloody diarrhea.

Hepatic – Increases in liver enzymes (LDH, SGOT, SGPT), hyperbilirubinemia. Rarely, cholestatic hepatitis.

Renal – Elevations of creatinine or BUN.

Central Nervous System – Headache, dizziness, fatigue.

Hemic and Lymphatic – Reversible leukopenia, neutropenia, thrombocytopenia and/or eosinophilia, bleeding and reases in prothrombin time have been reported. Reversible leukopenia (neutropenia) is more apt to occur in ents receiving prolonged therapy at high dosages or in association with drugs known to cause this reaction.

Serum Electrolytes – Individuals with liver disease or individuals receiving cytotoxic therapy or diuretics, were orted rarely to demonstrate a decrease in serum potassium concentrations with high doses of PIPRACIL.*

Musculo-Skeletal – Rarely, prolonged muscle relaxation.

Other – Superinfection, including candidiasis.

GE AND ADMINISTRATION: PIPRACIL* may be administered by the intramuscular route or intravenously by injec- or infusion. Dosage and route of administration should be determined by the severity of the infection and dition of the patient. The usual dosage for serious infections is 3 to 4 grams given every 4 to 6 hours as a 20 to 30 ute infusion administered intravenously.

The maximum daily dose usually administered to adults is 24 g/day, although higher doses have been used.

DOSAGE

Type of Infection	Usual Total Daily Dosage	Frequency of Administration
Serious infections such as septicemia, nosocomial pneumonia, intra-abdominal infections, aerobic and anaerobic gynecologic infections, and skin soft-tissue infections.	12-18 g I.V. (200-300 mg/kg)	Every 4 to 6 hours
Complicated urinary tract infections.	8-16 g I.V. (125-200 mg/kg)	Every 6 to 8 hours
Uncomplicated urinary tract infections and most community-acquired pneumonia.	6-8 g I.M. or I.V. (100-125 mg/kg)	Every 6 to 12 hours
Uncomplicated gonococcal urethritis.	2 g I.M.*	Single dose

*One gram of probenecid given orally 1/2 hour prior to injection.

Dosage In Renal Impairment

Creatinine Clearance mL/min.	Urinary Tract Infection (uncomplicated)	Urinary Tract Infection (complicated)	Serious Systemic Infection
>40	No dosage adjustment necessary		
20-40	No dosage adjustment necessary	9 g/day 3 g every 8 hrs.	12 g/day 4 g every 8 hrs.
<20	6 g/day 3 g every 12 hrs.	6 g/day 3 g every 12hrs.	8 g/day 4 g every 12 hrs.
Patients on Hemodialysis*	*Hemodialysis removes 30-50% of piperacillin in 4 hours; 1 g additional dose should be administered following each dialysis period.		6 g/day 2 g every 8 hrs.

For patients with renal failure and hepatic insufficiency, measurement of serum levels of PIPRACIL* will provide additional guidance for adjusting dosage.

Infants and Children – Dosages in infants and children under 12 years of age have not been established.

The average duration of PIPRACIL* treatment is from 7 to 10 days, except for gynecologic infections, in which it is from 3 to 10 days; the duration should be guided by the patient's clinical and bacteriological progress. For most acute infections, treatment should be continued for at least 48 to 72 hours after the patient becomes asymptomatic. Therapy for Group A beta-hemolytic streptococcal infections should be maintained for at least 10 days to reduce the risk of rheumatic fever of glomerulonephritis.

ADMINISTRATION

Intramuscular: When indicated by clinical and bacteriological findings, intramuscular administration of 6 to 8 g. daily of PIPRACIL* in divided doses, may be utilized for initiation of therapy and this route may be considered for maintenance therapy after clinical and bacteriologic improvement has been obtained with intravenous piperacillin sodium treatment. Administration should not exceed 2 g. per injection at any one site. This route has been used primarily in the treatment of patients with uncomplicated gonorrhea and urinary tract infections.

Adults and Children More Than 12 Years of Age: The reconstituted solution is given by deep intramuscular injection. The preferred site of injection is the upper outer quadrant of the buttock (i.e. gluteus maximus). Also may be given in the mid-lateral muscles of the thigh. The deltoid area should be used only if well developed, and then only with caution to avoid radial nerve injury. Intramuscular injection should not be made into the lower or mid-third of the upper arm.

Intravenous: The intravenous route should be used in the treatment of serious infections.

Direct Intravenous (Bolus) Injection: The vials should be reconstituted with 5 mL of suitable diluent listed below and the resulting solution should be injected slowly over a period of 3 to 5 minutes to help avoid vein irritation.

Intravenous Infusion: A dilution of at least 15 mL per gram is recommended to reduce potential for vein irritation. The reconstituted and diluted solution may be administered by intermittent or continuous drip. Intermittent infusion should be administered over a period of about 30 minutes. During intermittent infusion it is desirable to discontinue the primary intravenous solution. Any unused portion must be discarded. For continuous infusion the solution may be administered over a longer period of time.

RECONSTITUTION

For Intramuscular Use: Solutions for Reconstitution: Sterile Water for Injection, or if required
*Bacteriostatic Water for Injection,
**Lidocaine HC1 0.5 or 1% (without epinephrine) – For Intramuscular Use Only.

For Intravenous Use: Solutions for Reconstitution: Sterile Water for Injection, or if required,
*Bacteriostatic Water for Injection.
*Either parabens or benzyl alcohol.
**Lidocaine HC1 is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type.

RECONSTITUTION TABLE

Product Size	VOLUME OF Diluent to be added	Approximate Available Volume	Approximate Average Concentration
Vials 2 g	4.0 mL	5.0 mL	1 g/2.5 mL
3 g	6.0 mL	7.5 mL	1 g/2.5 mL
4 g	7.8 mL	10.0 mL	1 g/2.5 mL
Infusion Bottles			
3 g	15 mL	17 mL	
4 g	20 mL	23 mL	

The prepared solution may be further diluted to the desired volume with any of the solutions for intravenous infusion listed below.

The contents of the 3 and 4 g infusion bottles should be diluted to at least 15 mL per gram.

The appropriate quantity of reconstituted solution may be added to an intravenous bottle or bag containing any of the solutions for intravenous infusion listed below.

Solutions for Intravenous Infusion:

Intravenous Solutions:	Intravenous Admixtures:
5% Dextrose in Water [D_5W]	Normal Saline (+KCL 40 mEq).
0.9% Sodium Chloride (Normal Saline) [NS].	5% Dextrose/Water [D_5W] (+KCL 40 mEq).
Dextrose 5% and 0.9% Sodium Chloride [D_5NS].	5% Dextrose/Normal Saline [D_5NS] (+KCL 40 mEq).
Lactated Ringer's Injection, U.S.P.	Ringer's Injection, U.S.P. (+KCL 40 mEq).
Dextran 6% in 0.9% Sodium Chloride.	Lactated Ringer's Injection, U.S.P. (+KCL 40 mEq).

STABILITY OF SOLUTIONS: PIPRACIL* is stable in both glass and plastic containers when reconstituted with recommended diluents and further diluted with the indicated intravenous solution and intravenous admixtures.

Stability studies have demonstrated chemical stability (pH, potency and clarity) through 24 hours at room temperature and up to 72 hours refrigerated. Appropriate consideration of aseptic technique, however, recommends discarding unused portions after storage for 24 hours at room temperature or 48 hours refrigerated. If used as a multi-dose container, the vials must be reconstituted only with the bacteriostatic diluents noted above.

INCOMPATIBILITY: Because of chemical instability, PIPRACIL* should not be used for intravenous administration with solutions containing sodium bicarbonate

PIPRACIL* should not be added to blood products, protein hydrolysates or amino acids.

When PIPRACIL* is given concurrently with aminoglycosides, it is recommended that both drugs be used in full therapeutic doses, but administered separately. PIPRACIL* should not be mixed with an aminoglycoside in a syringe or infusion bottle, since this can result in inactivation of the aminoglycoside.

DOSAGE FORMS: PIPRACIL* (sterile, lyophilized piperacillin sodium) is available in vials containing amounts of piperacillin sodium equivalent to 2, 3 and 4 grams of piperacillin. Available in boxes of 12 vials.

Product Numbers: 2 g/vial – 3879-48 3 g/vial – 3882-49 4 g/vial – 3880-50

Available in 100 mL size infusion ("piggyback") bottles, containing sterile, freeze-dried piperacillin sodium powder equivalent to 3 and 4 grams of piperacillin. Boxes of 12 infusion bottles.

Product Numbers: 3 g/bottles – 3882-41 4 g/bottles – 3880-42

Piperacillin Sensitivity Discs impregnated with 100 ug of piperacillin are also available.

Storage:

PIPRACIL* vials and infusion bottles should be stored at controlled room temperatures of 15-30°C (59-86°F).

Piperacillin Sensitivity Discs should be refrigerated upon receipt. Product Monograph available on request.

*PIPRACIL is a trade mark of Lederle Piperacillin, Inc.

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TERENCE KENNEDY, MD(HON), MS, FRCS

Long-Term Results of Proximal Gastric Vagotomy

Proximal gastric vagotomy without drainage for duodenal ulcer was performed in 304 patients between 1969 and 1977. There was one operative death (0.3%) and two patients required secondary drainage (0.6%). Eleven patients died subsequently of unrelated causes. Follow-up 5 to 13 years after operation was conducted on 242 patients (80%). Of these, 141 were asymptomatic and 48 had only trivial symptoms, a success rate of 78%. Thirty-two patients had recurrent ulcer and 2 of them had Zollinger–Ellison syndrome. When these two were excluded, the recurrence rate was 12.4%. Two patients had duodenitis.

Seven patients had unexplained pain and some of them may ultimately be shown to have recurrence. Appreciable esophageal reflux was seen in eight patients. Other symptoms, nearly all mild, were dumping in one, diarrhea in seven and bile reflux in six.

Recurrent ulcer was treated by cimetidine initially in all 32 cases but ultimately by repeat vagotomy and antrectomy in 27, with no deaths and only one further recurrence (Zollinger–Ellison syndrome). After operative correction, the ultimate success rate (Visick grades I and II) was 90%.

Entre 1969 et 1977, une vagotomie gastrique proximale sans drainage a été pratiquée chez 304 patients. Un patient est décédé peropérativement (0.3%) et deux patients (0.6%) ont nécessité un drainage secondaire. Onze patients sont décédés par la suite, de causes n'ayant aucun rapport avec l'intervention. Un examen de contrôle a été effectué de 5 à 13 ans après l'opération chez 242 patients (80%). De ceux-ci, 141 étaient asymptomatiques et 48 n'avaient que des symptômes banals, pour 78% de bons résultats. Trente-deux patients avaient eu une récidive ulcéreuse et 2 souffraient du syndrome de Zollinger–Ellison. En excluant ces deux derniers le taux de récidive s'établit à 12.4%. Deux patients souffraient de duodénite.

Sept patients se plaignaient de douleurs inexpliquées et il est possible que, dans le futur, on constate chez eux une récidive. Un reflux gastrique appréciable a été observé chez huit patients. Les autres symptômes, presque tous bénins, comprennent "dumping" chez un, diarrhée chez sept et reflux biliaire chez six.

Les 32 cas de récidive ulcéreuse ont été traités initialement à la cimétidine mais 27 d'entre-eux ont finalement eu une deuxième vagotomie avec antrectomie; il n'y eut aucun autre décès et une seule autre rechute (un syndrome de Zollinger–Ellison). Après correction opératoire le taux final de bons résultats (les grades I et II à l'échelle de Visick) s'établit à 90%.

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Sixty-two years ago, André Latarjet[1] described the principal nerves of the lesser curve and 14 years ago, Amdrup and Jensen[2] and Johnston and Wilkinson[3] independently introduced the operation of parietal cell, highly selective or proximal gastric vagotomy without drainage. This operation has gradually been accepted in many countries; in many parts of the United Kingdom and Scandinavia it is now regarded as the operation of choice for chronic uncomplicated duodenal ulcer. The results, in terms of eliminating side effects, have been excellent[4] but over the long term, recurrence rates of about 20% have been reported.[5,6]

Patients and Findings

I performed my first proximal gastric vagotomy in 1969 and in my unit this operation has now been performed by various surgeons in 512 patients, with one operative death (0.2%). Primary drainage was required in 25 patients with stenosis of the gastric outlet. Of these operations, 304 were performed more than 5 years ago; 11 patients have died of various unrelated causes and 242 patients (80%) have now been followed up for between 5 and 13 years.

Recurrence

Ulceration recurred in 32 patients (13.2%), but 2 of these were shown to have Zollinger–Ellison syndrome and should probably be excluded, leaving a corrected recurrence rate of 12.4%. In published follow-up data, exceeding 5 years, of 1370 patients from seven different countries, the mean recurrence rate was 13.1%, so our experience appears to be average. Much lower recurrence rates have been reported by individual surgeons, giving their personal experience.[7] There are no published randomized, controlled data comparing recurrences after proximal gastric vagotomy with those 5 or more years after truncal vagotomy and drainage.

The clinical results were expressed as modified Visick gradings, in which grades I and II are regarded as successful, and are shown in Table I. The success rate was 78.1%, but it should be noted that 58% were graded Visick I, indicating that the patients had no symptoms of any kind. The Visick II patients had various vague symptoms, including a feeling of fullness in many cases. This was due to loss of receptive relaxation of the gastric fundus.

Side Effects

The objective when proximal gastric

Table I—Clinical Results of Proximal Gastric Vagotomy

Visick grade	No. of patients (n = 242)	Success (failure), %
I	141	78.1
II	48	
III	17	(21.9)
IV	36	

vagotomy was introduced was to eliminate troublesome side effects — namely dumping, bile reflux and vomiting and, in particular, postvagotomy diarrhea. The number of side effects is shown in Table II; in only one patient were the symptoms sufficiently severe to warrant a Visick grading other than II, which indicates qualified success. Of the seven who had diarrhea, this symptom followed cholecystectomy in two; the combination of cholecystectomy and vagotomy is known to be diarrheogenic. It should be remembered that many healthy patients with neither ulcer nor operation experience similar symptoms from time to time.[4]

Failures

The failures are analysed in Table III. The absolute failures (Visick grade IV) include the 32 patients with recurrence already noted and 2 patients with duodenitis but no ulceration. Two other patients had gastric retention in the early postoperative period and required drainage; they subsequently did well.

The qualified failures (Visick grade III) were a heterogeneous group. In seven there was abdominal pain but no endoscopic or other evidence of recurrence. Some of these patients as well as the two with duodenitis may ultimately be found to have a recurrent ulcer. One patient had moderate diarrhea, but it was probably due to the irritable bowel syndrome. The most important problem has been esophageal reflux. It is scarcely surprising that hiatus hernia or reflux may occur after the manipulation required to bare at least 5 cm of esophagus. It is tempting, and indeed easy, to add a Nissen fundoplication[8] but we found three instances of lesser curvature necrosis, in patients operated on after this series was completed, when proximal gastric vagotomy and fundoplication were combined.[9] This may have been due to the "bloat syndrome" and could perhaps have been avoided by ensuring that the wrap around was "floppy". Another alternative is the Hill procedure as modified by Oster and colleagues.[10]

Comments

What can be done for the failures? Most experienced surgeons recognize that dumping, diarrhea and bile reflux can be extremely difficult to treat, but in this series the major problem was the management of recurrent ulcer. We have had only limited success with cimetidine and ranitidine and more than half of our patients have eventually required a second operation. The Nashville school[11] has shown that vagotomy with antrectomy as a primary procedure has a very low recurrence rate so it is rational to treat recurrent ulcer by repeat vagotomy and antrectomy.[12] We used this procedure in 104 patients after all types of vagotomy; there was one operative death, in an emergency procedure, and only two further recurrences. Thus, recurrent ulcer can be well controlled by adequate further surgery. After correction of the failures by medical or surgical treatment, the ultimate clinical grading shows a 90% success rate (Table IV).

The somewhat high recurrence rate that we have experienced leads us to ask whether there are any technical modifications that should be applied. We did not employ intraoperative tests of completeness of vagotomy, although evidence supporting the use of Burge[13] or Grassi tests[14] appears convincing.

We have not used proximal gastric vagotomy for gastric ulcer and perforated or bleeding ulcer often enough to make any worthwhile comment. For pyloric stenosis, we initially added pyloroplasty but we have now combined proximal gastric vagotomy with duodenoplasty[15] in 44 patients; in 5 of these, the ulcer ultimately recurred but only 1 had further obstructive symptoms.

From this experience we conclude that proximal gastric vagotomy is a safe procedure and the undesirable side effects of truncal vagotomy with drainage are virtually eliminated. Esophageal reflux may be a problem and its management is still not clearly defined. The great problem is recurrent ulcer but this can be controlled by either medical or surgical treatment so that the ultimate failure rate is only 10%. Proximal gastric vagotomy is surely here to stay.

Table II—Late Side Effects after Proximal Gastric Vagotomy in 242 Patients Followed up for 5 to 13 Years

Side effect	No. (%)
Dumping	1 (0.4)
Diarrhea	7* (2.9)
Bile reflux	6 (2.5)

*Two followed cholecystectomy.

Table IV—Corrected Clinical Grading (after Treatment of Failures), 5- to 13-Year Follow-up

Visick grade	No. of patients	Success (failure), %
I	162	90
II	55	
III	21	(10)
IV	4	

Table III—Causes of Failure

Cause	Visick grade III (n = 17)	Visick grade IV (n = 36)
Unexplained abdominal pain	7	–
Esophageal reflux	8	–
Diarrhea	1	–
Psychogenic	1	–
Recurrent ulcer	–	32*
Duodenitis	–	2
Retention	–	2

*2 with Zollinger–Ellison syndrome.

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Arterial Injuries

The authors review arterial injuries in 68 patients treated at Maisonneuve-Rosemont Hospital in Montreal between 1975 and 1982. Penetrating trauma caused 54.4% of these injuries, which consisted of either laceration or intimal tear with thrombosis. Arterial injuries of the extremities were predominant (58.8%). Associated injuries were frequent. Surgical repair was effected in 60 patients. End-to-end anastomosis, angioplasty and venous or prosthetic bypass grafting were the techniques used. Postoperative complications occurred in 37% of the patients. Overall mortality was 19% and was related mainly to aortic injury. The amputation rate for arterial injuries of the extremities was 15%. Prompt recognition and treatment of arterial injuries are important in order to achieve the best results.

Durant la période de 1975 à 1982, 68 patients furent traités pour traumatisme artériel à l'hôpital Maisonneuve-Rosemont. Les plaies pénétrantes causèrent 54.4% de ces traumatismes. La lacération partielle ou complète et la rupture intimale avec thrombose furent les deux types de lésions rencontrées. La proportion de traumatisme artériel des extrémités fut de 58.8%. Les traumatismes associés furent fréquents. Une correction chirurgicale fut pratiquée chez 60 patients. Les techniques utilisées furent: l'anastomose termino-terminale, l'angioplastie et le bypass veineux ou synthétique. Le taux de complications postopératives fut de 37%. La mortalité totale fut de 19% et en relation avec les traumatismes aortiques. Le taux d'amputation pour les traumatismes artériels des extrémités fut de 15%. Le diagnostic et le traitement des traumatismes artériels doivent être des plus précoces si l'on veut obtenir des résultats favorables.

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This study reviews 68 cases of arterial trauma treated at the Maisonneuve-Rosemont Hospital in Montreal from 1975 to 1982. Most patients were less than 50 years old. The anatomical distribution of the injuries is illustrated in Fig. 1. Arterial injuries of the extremities were predominant (58.8%) followed by those of the abdomen, neck and thorax.

The two main types of arterial injury encountered were partial or complete laceration (64.7%) and intimal tear with thrombosis (33.8%). Penetrating injuries resulting from gunshot and stab wounds and motor vehicle accidents were responsible for 54.4% of the cases.

Hypovolemic shock was frequently present. Injuries to the central nervous system, abdominal contents and bones were common. The clinical presentation was acute in all patients but one who had a chronic pseudoaneurysm of the right iliac artery caused by blunt abdominal trauma. Trauma to arteries of the trunk was characterized by hypovolemic shock associated with multiple organ injuries. Varying degrees of acute ischemia and hemorrhage were the two classic accompaniments of arterial injuries to the extremities.

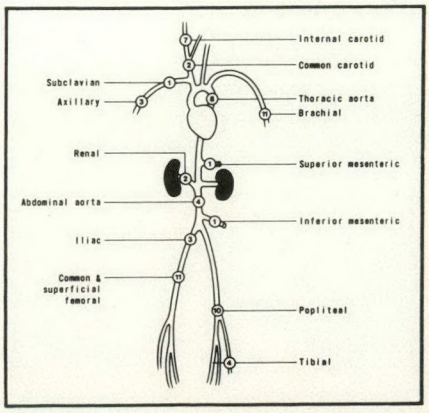

FIG. 1—Anatomical distribution of arterial injuries.

Surgical repair was carried out in 60 patients; in the other 8, the clinical situation precluded any arterial reconstruction. The surgical techniques used were débridement and end-to-end anastomosis (16 patients), angioplasty (8), saphenous bypass grafting (16), prosthetic bypass grafting (13), ligation (3), nephrectomy (2) and exploration (2). All arterial injuries in the limbs were treated with the first two techniques. Prosthetic material was usually required to repair aortic injuries.

There were 25 (37%) postoperative complications and 13 deaths (19%) (Table I). These high rates well reflect the severity and the magnitude of these injuries. The mortality of 19% was related mainly to aortic injuries. Arterial injuries of the extremities were associated with a 15% amputation rate.

To some extent, each anatomical region had its own features, and accordingly they will be reviewed separately.[1]

Carotid Arteries

A direct blow to the neck and severe hyperextension of the cervical spine were

Table I—Complications and Mortality

Complication/death	No.
Death	13
Neurologic sequelae	
Central	4
Peripheral	7
Major amputation	6
Compartment syndrome	3
Causalgia	2
Crush syndrome	1
Pulmonary embolism	1
Pancreatic fistula	1

responsible for carotid (common and internal) artery injuries in eight patients. These injuries produced intimal tears with secondary thrombosis. When first seen, the majority of these patients already had a neurologic deficit, indicating the presence of the lesion. In the presence of a recent deficit, surgery was carried out only in one patient with a circumferential intimal tear of the carotid bifurcation and partial thrombosis. One patient had a stab wound of the common carotid artery. Surgical treatment in this case included lateral suture of the carotid artery. Important neurologic sequelae ensued in three patients (33%).

Thoracic Aorta

In a group of seven patients with deceleration injury, four who were in stable condition with contained rupture of the thoracic aorta had a successful operation. In contrast, three patients with free aortic rupture died of hypovolemic shock despite aggressive resuscitation and attempted surgical repair. Early diagnosis and treatment are most important if this situation is to be avoided. Surgical treatment included grafting the defect; a temporary shunt was used in most patients. One patient with a stab wound of the aortic arch is also reported.

Abdominal Arteries

Penetrating injuries predominated (56.5%) in these 11 patients with abdominal arterial trauma. Associated injuries occurred in all cases and involved the majority of intra-abdominal organs. Hypovolemic shock was frequent (63.6%). Surgical treatment included aortic repair in two patients, nephrectomy in two and angioplasty in one patient. Iliac artery bypass was performed in three patients. Two patients with gunshot wounds of the aorta died during the operation. Mortality was 45.4% and was related to prolonged and severe preoperative shock associated with aortoiliac injuries.

Arterial Injuries to the Extremities

The mechanism of injury and the types of arterial trauma were identical in the upper and lower extremities in 40 patients. Arterial laceration occurred in 66.7% of the cases and intimal injury with thrombosis in 33.3%. A high incidence of fractures and soft-tissue trauma was noted in association with arterial injuries of the extremities.[2] This combination had a negative impact on the outcome in these patients. Soft-tissue injury and associated fractures carried, respectively, 23.5% and 33% amputation rates while in isolated arterial trauma the amputation rate was only 11%. Surgical treatment consisted of débridement and either end-to-end anastomosis or saphenous vein grafting. Peripheral nerve injuries occurred in 40% of the patients with arterial injuries of the upper extremities leading to chronic disability in 26% of them.

Angiography was done in 48.5% of the patients. Acute ischemia and signs of vascular involvement were the usual indications. The overall accuracy of the technique was 97%. Indications for angiography are relative as in patients with a single injury and acute arterial insufficiency. In contrast, the indication is strong in multiple injuries of one limb combined with arterial insufficiency and in patients with preexisting atherosclerotic disease and possible arterial injury. Suspected thoracic aortic rupture is an absolute indication for angiography and a positive angiogram is essential before embarking on a thoracotomy. Angiography may be detrimental to those patients with active bleeding and obvious arterial injury.

Peripheral arterial injury associated with limb fractures has been a subject of controversy in regard to which injury should be treated first. Eleven such cases occurred in our series. In five patients, the vascular repair was carried out before and in six patients after the orthopedic procedure. Complication and amputation rates were comparable. The amputation rate was 20% in patients whose vascular injury was repaired first and 33% in the others; this is not statistically significant. Despite the small numbers, these results tend to support the concept that the order of repair must be chosen for each individual case. The duration of ischemia remains the important factor in this selection. In the first 2 hours after arterial trauma, the orthopedic procedure can be carried out first, but after 4 to 5 hours of ischemic time, revascularization becomes imperative to avoid the sequelae and complications of prolonged acute ischemia. Close cooperation between the orthopedic and vascular teams is essential to achieve the best results. The Roger Anderson or the Hoffman device was used in all these patients.[3]

Associated peripheral nerve injuries were found in 40% of patients with arterial trauma to the upper extremities and in 12% with arterial injury in the lower extremities. Long-term neurologic sequelae were present in at least 12.5% of the patients with arterial injuries to the limbs.[4] Treatment of these injuries should be carried out at the same time if feasible. Proximal nerve injuries usually carry a poor prognosis, while distal lesions offer the best chance of recovery.

Of 40 patients with arterial injuries of the limbs, 6 had associated venous injuries with a predilection for the popliteal segment. Repair was carried out in four patients and extensive damage precluded any reconstruction in the other two patients. The amputation rate for this group of six patients was 33%. In one patient, who was in the ligation group, the amputation was directly related to venous outflow occlusion and massive edema. Although these numbers are too small to draw any firm conclusion, major vein ligation seems to carry a substantial amputation rate. Venous repair is probably as important as arterial repair at least in critical locations such as the popliteal area.

Crushing injuries, more than 6 hours of ischemia and associated venous injuries are the usual indications for fasciotomy at the time of the arterial repair. Three patients were in this category. In four others without these predisposing factors, a compartment syndrome developed within 48 hours of revascularization. Fasciotomy through small skin incisions offers good decompression and has a minimal effect on soft tissues, which are often severely traumatized. Fibulectomy, although theoretically sound, may be ill-advised in these circumstances.

The overall amputation rate in arterial injury of the limbs was 15%. The lower limbs were involved in all but one amputation. Analysis of the causes of amputation underlines some important factors such as delay in diagnosis, wound sepsis and graft failure (Table II). Delay in diagnosis occurred twice and led to amputation in both cases. These two patients were transferred to our institution 3 days and 22 hours, respectively, after injury.

Wound sepsis was usually secondary to severe soft-tissue trauma associated with multiple fractures. Due to heavy contamination, local edema and devitalized tissues, infection supervened. This necessitated amputation in two patients.

Graft failure was responsible for one amputation despite early re-exploration

Table II—Causes of Major Amputation

Site	No.	Cause
Axillary	1	Delay in diagnosis (3 d)
Femoral	1	Extensive damage precluding repair, primary amputation
Popliteal	4	Crush syndrome
		Wound sepsis
		Delay in diagnosis, venous injury, wound sepsis
		Graft failure, wound sepsis

of the arterial repair. One of the most difficult decisions and one that requires experience is when to amputate rather than revascularize the limb,[5] particularly in the case of extensively injured limbs with loss of soft tissue and skin and with neurovascular damage. When in doubt, a primary reconstruction should be attempted. Amputation may be done as a secondary procedure if necessary.

The treatment of vascular trauma continues to be an exciting challenge and requires much ingenuity. Application of the modern principles of treatment has greatly reduced the morbidity and mortality associated with this condition.

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Doppler Waveform Analysis versus Segmental Pressure and Pulse-Volume Recording: Assessment of Occlusive Disease in the Lower Extremity

In a prospective study, the accuracy of combined segmental pressure measurements and pulse-volume recordings was compared with Doppler waveform analysis in evaluating peripheral arterial occlusive disease.

Before arteriography, 50 patients (100 limbs) underwent vascular assessment which included measurement of the segmental pressure and pulse volume at the thigh, calf and ankle. Analogue Doppler waveform tracings were obtained from the femoral, popliteal and tibial arteries and used to calculate the pulsatility index and inverse damping factor. Results of each method were assessed by independent observers and compared with the arteriographic data.

No appreciable difference was demonstrated between the two methods, both giving an overall accuracy in the 90% to 95% range. Both accurately predicted the severity of iliac and superficial femoral artery obstruction and distinguished iliac from proximal disease of the superficial femoral artery. Outflow disease (tibial arteries) was better assessed by measurement of segmental pressures than by Doppler waveform analysis or pulse-volume recording alone.

Dans une étude prospective, la précision obtenue en associant la mesure de la pression segmentaire et l'enregistrement du volume systolique a été comparée à celle de l'analyse des ondes Doppler comme méthode d'évaluation des oblitérations des artères périphériques.

Avant l'artériographie, 50 patients (100 membres) ont été soumis à une évaluation du système vasculaire comprenant la mesure de la pression segmentaire et du volume systolique au niveau de la cuisse, du mollet et de la cheville. Les tracés correspondants des ondes Doppler obtenus des artères fémorales, poplitées et tibiales ont été utilisées pour calculer l'indice de pulsatilité et le facteur de modulation inverse. Les résultats de chaque méthode ont été appréciés par un observateur indépendant qui les a comparés aux données artériographiques.

La précision globale rattachée à l'une ou l'autre des deux méthodes variait de 90% à 95% et ne différait pas de façon appréciable. Les deux méthodes sont capables de prédire avec précision la gravité des oblitérations des artères iliaques et fémorales superficielles et de distinguer entre les foyers iliaques et fémoraux superficiels d'obstruction. L'obstruction de l'artère tibiale s'évalue mieux par la mesure de la pression segmentaire que par l'analyse des ondes Doppler ou de l'enregistrement du volume systolique seul.

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Noninvasive evaluation has recently assumed an increasing role in the management of patients with peripheral vascular disease. In the 20 years since the advent of the first Doppler velocity detector, many types of equipment for noninvasive investigation of vascular problems have been developed. If the vascular surgeon is to utilize data obtained from these instruments to make critical clinical decisions, it is essential that he know the limits of their reliability. The combination of segmental pressure measurements and pulse-volume recordings is perhaps the most common approach used at present to evaluate the arterial circulation to the lower limbs. Various authors[1-3] have reported excellent results with this technique. Others, [4,5] using frequency analysis of Doppler signals, have also claimed that the method will reliably assess arterial occlusive disease in the peripheral vessels.

We have recently concluded a prospective study, comparing the accuracy of segmental pressure and pulse-volume recording with that of Doppler waveform analysis in a group of patients who subsequently underwent angiographic evaluation.

Methods

Before arteriography, 50 patients (100 limbs) underwent assessment in the vascular laboratory. The assessment consisted of: (a) measurement of the segmental pressures and pulse volume at the thigh, calf and ankle, using a Life Sciences pulse-volume recorder (Life Sciences Inc., Greenwich, Conn.), and an exercise test; (b) Doppler waveform analysis of the femoral, popliteal and tibial arteries using a Bach-Simpson DFA-10 frequency analyser (Bach-Simpson Ltd., London, Ont.). Single-plane arteriography was then performed using standard methods.

The interpretations of the segmental pressure and pulse-volume recordings and Doppler waveform analysis were carried out by different individuals independently, who had no knowledge of the results of the other procedure. The findings were then compared to those from arteriography with respect to specificity, sensitivity and accuracy.

Segmental Pressure Measurement

Segmental pressures were recorded conventionally with a Doppler flow probe at the ankle and appropriate cuffs at the brachial, thigh, calf and ankle levels. After 1 minute of treadmill exercise, the ankle pressure measurements were repeated at 1-minute intervals until baseline pressures were restored. Our criterion for the presence of significant stenosis was a pressure gradient of 20 mm Hg between segments or an ankle–brachial index less than 0.8. An ankle–brachial index less than 0.5 was considered indicative of multisegment disease. Postexercise recovery time at the ankle level was also used to indicate the degree of ischemia present.

Pulse-Volume Recordings

The criteria for the presence of occlusive disease with this technique are related to waveform contour and amplitude. The presence of notable proximal obstruction is signalled by flattening of the anacrotic limb, rounding of the crest and loss of the dicrotic notch or a decrease in amplitude, or both. Further, the fact that the calf pulse-volume recording has a greater amplitude than that of the thigh, except in the presence of superficial femoral obstruction, was used to distinguish iliac from proximal disease of the superficial femoral artery.

Doppler Waveform Analysis

Criteria for the presence of occlusive disease by this method were based on the waveform contour, the pulsatility index and the inverse damping factor (DF^{-1}). As with pulse-volume recording, the velocity waveform will have a lower, flattened peak, a decreased upstroke and no reversed flow over a diseased vessel. A pulsatility index of 6 or more at the femoral level was considered indicative of a normal iliac segment, while a value less than 5 implied substantial iliac stenosis. A DF^{-1} of less than 1 was considered indicative of significant disease in that segment (superficial femoral or tibial).

Specificity, Sensitivity, Accuracy

The iliac, superficial femoral and outflow (tibial arteries) segments of the arteriograms were classified as (a) no significant stenosis, (b) less than 50% stenosis, (c) 50% to 99% stenosis and (d) occlusion.

The result of the combined segmental pressure and pulse-volume recordings and that of the Doppler waveform data for each segment were analysed and compared with the arteriographic findings for specificity, sensitivity and accuracy. Specificity was defined as the number of negative noninvasive tests divided by the number of arteriograms that appeared normal or showed less than 50% stenosis. Sensitivity was defined as the number of positive noninvasive tests divided by the number of arteriograms showing 50% to 100% stenosis. Accuracy was defined as the total number of positives plus negatives divided by the total number of limbs examined.

Results

The patient illustrated in Figs. 1 to 3 with an isolated unilateral iliac lesion is cited as an example of the findings on segmental pressure and pulse-volume recording and on Doppler waveform analysis. Fig. 1 demonstrates an important segmental pressure gradient at the thigh level and the pulse-volume recording shows the typical changes of an occlusive iliac lesion (decreased amplitude and abnormal contour of the thigh and

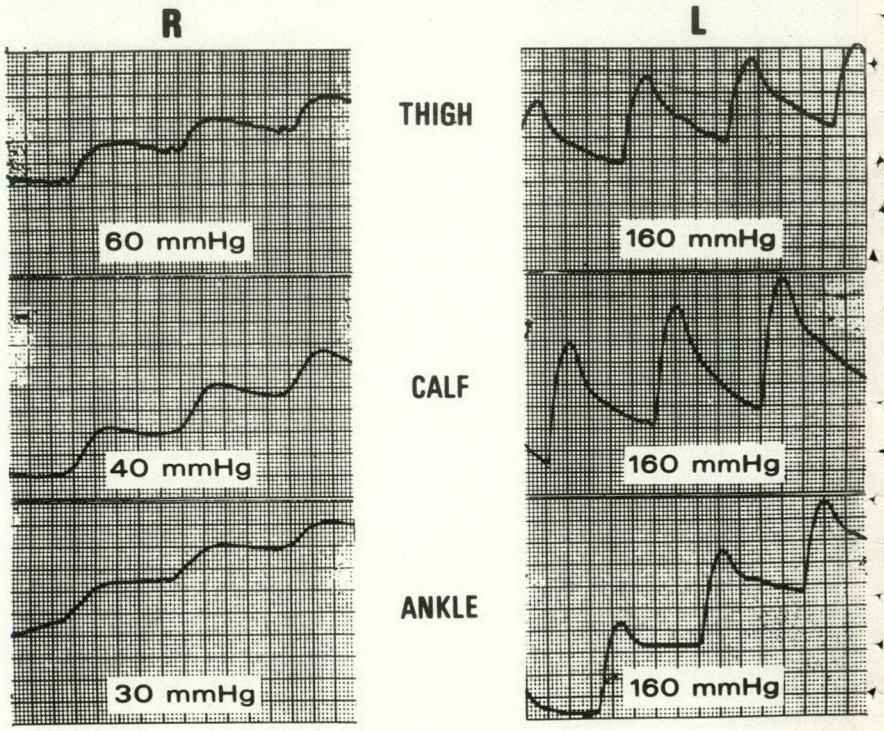

FIG. 1—Isolated iliac artery occlusion. Typical segmental pressure and pulse-volume recording.

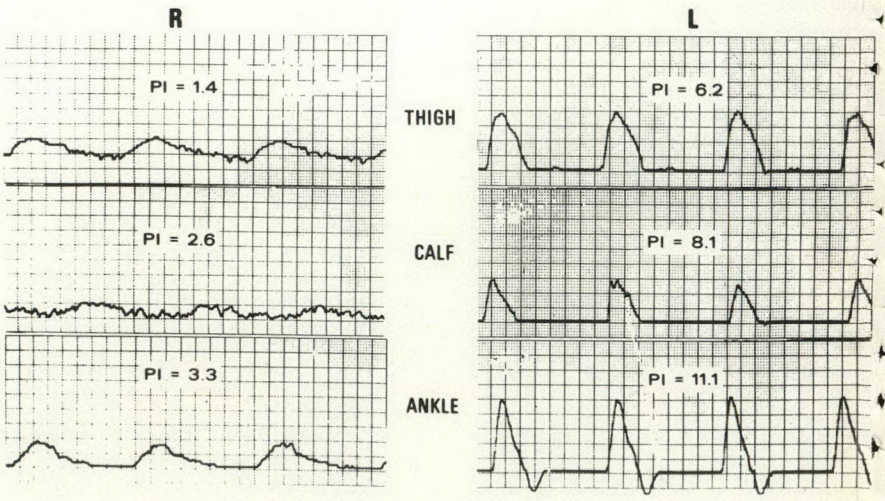

FIG. 2—Doppler waveform analysis on same patient as Fig. 1.

calf tracings, calf showing greater amplitude than thigh). Fig. 2 demonstrates the Doppler waveform changes in the same patient. The waveform is markedly altered, compared with the other leg, the pulsatility index is diminished at the femoral level while the DF^{-1} distally is normal (greater than 1).

The results in the 100 limbs we analysed are summarized in Table I. They indicate that both techniques are accurate in identifying obstructive lesions greater than 50% when compared to our "gold standard" of arteriography. Both methods reliably distinguished iliac disease from superficial disease. In fact, the lower specificity at the iliac level may imply the detection of so-called occult iliac stenosis not adequately seen on single-plane angiograms. We did find that Doppler waveform analysis was not as accurate in assessing the outflow but the differences were not significant.

Discussion

Over the past 6 years we have used the combination of segmental pressure measurements and pulse-volume recordings to evaluate arterial occlusive disease in the lower limb. With the advent of Doppler waveform analysis as an alternative method, we elected to evaluate prospectively both approaches and thus determine the limits of reliability of each and whether or not one was superior to the other in delineating the presence of obstruction of the iliac, superficial femoral and tibial vessels.

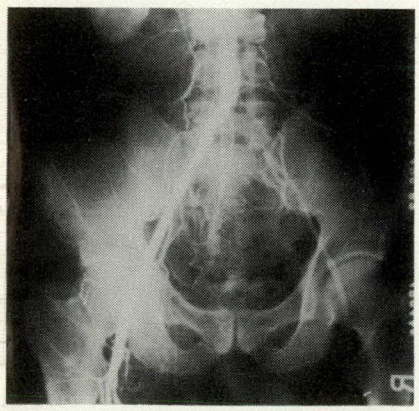

FIG. 3—Arteriogram of same patient, with unilateral iliac artery occlusion. Distal vessels (not shown) were patent.

The criteria and methods for measuring segmental pressure and pulse volume have been well documented. However, the terminology of pulsatility index and inverse damping factor (DF^{-1}) deserves further clarification. Waveform analysis is the best method for processing Doppler signals. A normal Doppler waveform is triphasic (forward flow, reversed flow and then again forward flow). If an occlusive lesion is present, then the waveform distal to it will be diminished. In order to eliminate variations of the waveform caused by technical factors, several investigators[4-6] have devised the pulsatility index to quantify the Doppler waveform. The pulsatility index is the peak height of a wave divided by the mean height. The DFA-10 frequency analyser calculates these numbers automatically and prints them as the waveforms are recorded. Hemodynamically important stenosis at the femoral level is indicated if the pulsatility index is 5.0 or less. Normally, the index increases with progression distally in the leg. This has been quantified by a second numerical index, the damping factor, which is the proximal pulsatility index divided by the distal pulsatility index.[7] To conform to the convention of decreasing indices with increasing disease severity, the term is expressed as the inverse damping factor (DF^{-1}). If the DF^{-1} is less than 1, then disease is present in that arterial segment. Therefore, with Doppler waveform analysis, the diagnosis of occlusive vascular disease can be ascertained by inspecting the analogue waveform at the femoral, popliteal and tibial vessels and by calculating the pulsatility index and DF^{-1}. In this study, all procedures were carried out by the same technician on each patient at the same examination. The data were then interpreted independently by different evaluators before the angiograms were studied for comparison.

The results of the study clearly demonstrate that both approaches offer a high degree of accuracy at the iliac and superficial femoral levels. Both pulse-volume recording and Doppler waveform analysis distinguished accurately iliac from proximal obstruction of the superficial femoral artery even when both were present in the same limb. Evaluation of the tibial outflow segment appeared better with segmental pressure and pulse-volume recording, primarily because severe proximal disease tended to damp both the pulse-volume recording and Doppler waveform tracings alone whereas segmental pressure measurements could still show a gradient between the calf and ankle, and an ankle–brachial index below 0.3 generally indicated poor outflow below the knee.

In most instances, single-plane films only were taken and only occasionally were oblique films used to assess the iliac vessels. The limitations of arteriography in assessing aortoiliac disease have been documented and many surgeons believe that stenoses in these segments are routinely underestimated. In 1971, Moore and Hall[8] outlined some of the physiologic problems in interpreting aortoiliac disease from arteriography. Despite these limitations, we still rely on arteriography in planning the therapeutic approach and because it is the current "gold standard", we felt justified in using it for comparison with our data. Some of the false-positive results obtained from both methods at the iliac level may in fact reflect a greater sensitivity of these noninvasive tests to so-called occult iliac disease.

Table I—Results Obtained with Combined Segmental Pressure and Pulse-Volume Recording (SP/PVR) and Doppler Waveform Analysis (DWA) Compared with the Arteriographic Data for Each Segment

Segment	SP/PVR, %	DWA, %
Iliac		
Sensitivity	95.1	94.9
Specificity	83.3	88.8
Accuracy	91.5	92.9
Superficial femoral artery		
Sensitivity	93.3	92.8
Specificity	85.2	96.2
Accuracy	89.5	94.4
Outflow		
Sensitivity	100.0	80.0
Specificity	66.0	50.0
Accuracy	96.4	78.8

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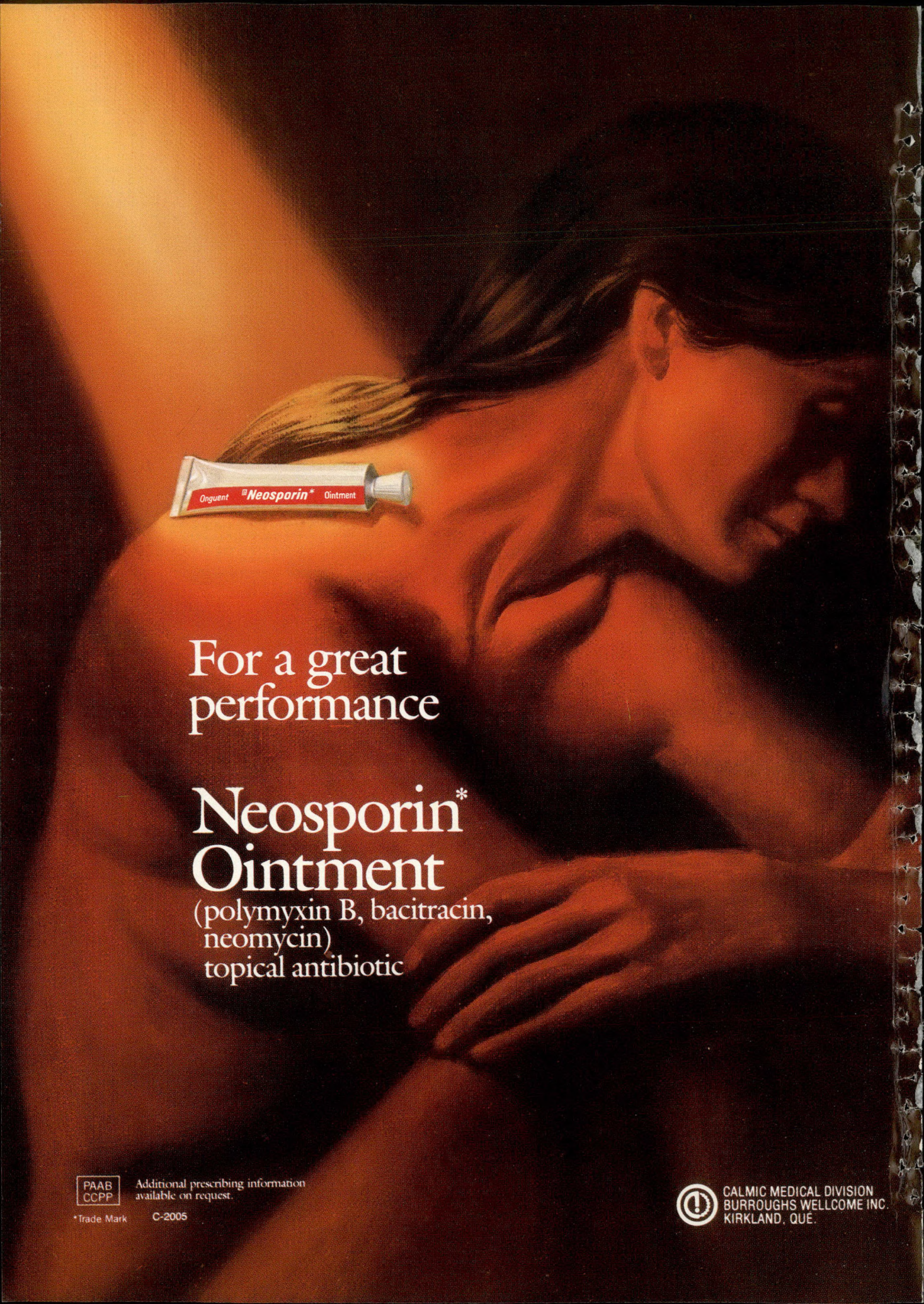

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Ventricular Function following Mitral Valve Surgery: Assessment Using Radionuclide Ventriculography

The effects of mitral valve replacement or commissurotomy on cardiac function were studied using radionuclide ventriculography in 13 patients with chronic mitral stenosis and in 8 with chronic mitral regurgitation, before and after mitral valve surgery. The stenosis resulted from rheumatic heart disease in all instances while regurgitation was due to mitral valve prolapse in three patients and rheumatic heart disease in five. Fourteen patients had a Carpentier–Edwards valve inserted and 4 a Lillehei–Kaster disc valve. Three patients with mitral stenosis had an open commissurotomy.

All patients underwent supine-rest and symptom-limited exercise radionuclide ventriculography shortly before and 6 to 12 months after operation. The data obtained showed that left ventricular function remained unchanged postoperatively in patients with mitral stenosis but deteriorated in those with mitral regurgitation. Right ventricular function improved postoperatively in those with mitral stenosis but remained unchanged in patients who had regurgitation.

Les effets sur la fonction cardiaque d'un remplacement de valvule mitrale ou d'une commissurotomie ont été étudiés chez 13 patients souffrant de sténose mitrale chronique et chez 8 patients ayant une régurgitation mitrale chronique au moyen d'une ventriculographie isotopique pratiquée avant et après chirurgie valvulaire. La sténose était le résultat d'une cardite rhumatismale dans tous les cas alors que les régurgitations étaient dues à un prolapsus de la valvule mitrale dans trois cas et à une cardite rhumatismale dans cinq cas. Quatorze patients ont reçu une prothèse Carpentier–Edwards et 4 une valvule à disque Lillehei–Kaster. Trois patients porteurs d'une sténose mitrale ont subi une commissurotomie ouverte.

Tous les patients ont subi une ventriculographie isotopique au repos, en position couchée, et à l'effort limité par les symptômes, avant, et de 6 à 12 mois après l'opération. Les résultats obtenus montrent que la fonction ventriculaire gauche est demeurée inchangée en postopératoire chez les patients qui avaient une sténose mitrale alors qu'elle s'est détériorée chez ceux qui avaient une régurgitation mitrale. La fonction ventriculaire droite s'est améliorée en postopératoire chez ceux qui avaient une sténose mais elle est demeurée inchangée chez les patients souffrant de régurgitation.

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The left ventricular ejection fraction at rest may be either normal or decreased in the presence of mitral stenosis.[1-8] Studies examining exercise left ventricular function usually demonstrate hemodynamic abnormalities.[9-12] Whether reduced left ventricular function is due to a decrease in diastolic filling or to intrinsic myocardial dysfunction has not been firmly established.[2-4,6,8,13-17] Left ventricular ejection fraction at rest is usually maintained in mitral regurgitation due to adjustments in left ventricular and left atrial mechanics[18-22] so that a depressed value in such patients indicates a markedly abnormal ventricle. Mitral valve replacement at this stage may be associated with further deterioration in left ventricular function or a decrease in operative survival.[7,23-26] Right ventricular function has not been extensively evaluated for either mitral stenosis or regurgitation.

The purpose of this study was to compare the effects of mitral valve replacement or commissurotomy in patients with mitral stenosis and those with mitral regurgitation. Equilibrium radionuclide ventriculography provides an excellent noninvasive tool to examine rest and maximal exercise biventricular function.[27,28]

Patients and Methods

Included in the study were 21 patients, 13 (11 women, 2 men, group 1) in whom mitral stenosis was the predominant valvular lesion and 8 (4 women, 4 men, group 2) in whom mitral regurgitation was predominant. The mean age for group 1 patients was 58 years (range from 40 to 73 years) and for group 2, 54 years (range from 39 to 68 years).

The cause of the condition was established in all patients by cardiac catheterization and M-mode or two-dimensional echocardiography. The mitral stenosis in all group 1 patients was due to rheumatic cardiac disease. The mitral regurgitation in group 2 patients was due to rheumatic cardiac disease in five patients and to mitral valve prolapse in three.

In both groups the patients' hemodynamic condition was severe — luminal diameter of 1 cm^2 or less in all group 1 patients as determined by the Gorlin method and regurgitation demonstrated angiographically in group 2. No patient had significant coronary artery disease (25% or more narrowing of one or more coronary arteries).

In group 1, 10 patients received new mitral valves (Carpentier–Edwards bioprosthetic porcine valve in 8, Lillehei–Kaster eccentric monocuspid disc valve in 2) and 3 patients had an open mitral commissurotomy. In group 2, all patients

underwent mitral valve replacement (Carpentier–Edwards in six and Lillehei–Kaster in two).

Mitral valve disease had been present in all patients for at least 5 years and in most for many years. Patients underwent preoperative assessment within the 3 months before operation. Postoperative assessment was conducted 6 to 12 months after the surgical procedure. Diuretic therapy was reduced at the time of postoperative assessment in 10 of 13 patients with mitral stenosis and 4 of 8 with mitral regurgitation. All patients were required to undergo at least one 3-minute stage of supine bicycle exercise at a workload of 25 watts.

Twenty-eight healthy men with a mean age of 54 years (range from 34 to 65 years) served as controls. No one was taking regular medication. In all, the findings of functional inquiry, physical examination, exercise stress electrocardiogram and thallium-201 scintigraphy were normal. Wall motion was normal during exercise radionuclide ventriculography.

In all group 1 patients, the left ventricular ejection fraction, derived from a single right anterior oblique projection at the time of cardiac catheterization, was more than 50%; it was less than 50% in four group 2 patients, as determined at the time of ventriculography.

Radionuclide Ventriculography

Electrocardiographically multigated equilibrium radionuclide ventriculography was carried out with the patient supine at rest and during symptom-limited exercise. After in-vivo labelling of erythrocytes with 20 mCi of technetium-99m pertechnetate, cardiac scintigraphy was performed in the left anterior oblique position that best isolated the left ventricle. All images were collected for 2 minutes using a conventional Anger scintillation camera equipped with a high-sensitivity parallel-hole collimator interfaced to a dedicated medical computer system (Ohio Nuclear model 460; Technicare International, Cleveland, Ohio).[29] Data were collected in a continuous electrocardiographic synchronized mode with 16 frames spanning the cardiac cycle. Patients began supine exercise with an initial workload of 25 W, which was increased by 25 W every 3 minutes until symptoms were produced. Data were analysed using a mobile medical computer (Ohio Nuclear model 550). As previously described,[30] the left ventricular ejection fraction was derived by first identifying a background region of interest, approximately 50 to 100 pixels along the inferolateral left ventricular free wall of the end-systolic frame. After smoothing and background subtraction, a region of interest was then drawn manually around the left ventricle at end-systole and end-diastole (previously identified from the left ventricular time-activity curve), using an endless-loop ciné display to improve edge detection. This was performed on three separate occasions and an average of the three counts for each of the frames was used to calculate the ejection fraction.

Determination of the right ventricular ejection fraction was based on a previously described technique.[28] After subtraction of background activity previously identified along the left ventricular free wall, right ventricular end-systolic and end-diastolic regions of interest were manually outlined. The superior right ventricular edge was considered to border on a parallel line drawn from the mitral valve plane in both diastole and systole.

Analysis of variance shows that for the left ventricle a change in ejection fraction of 5% (absolute value) or more was significant. For the right ventricle, a change of 11% (absolute value) or more in ejection fraction was considered significant.

The percentage change in radioactive counts from rest to exercise at end-systole and end-diastole was used to determine changes in cardiac volume.[31]

Statistical Analysis

Student's *t*-test for paired and unpaired samples was used to determine significant changes in hemodynamic parameters. Two-way analysis of variance was used to determine intraobserver and interobserver variance for left and right ventricular ejection fractions from 25 previously obtained resting studies in patients with coronary artery disease. Variance was defined as the error due to observer bias plus the random error of the method. The largest variance obtained from intraobserver and interobserver sampling was used to define a significant change upon introduction of an intervention. Probability of 5% or less was considered significant.

Results

Atrial fibrillation was present in 9 of the 13 group 1 patients preoperatively and it developed postoperatively in 2 others. In group 2, six of the eight patients had atrial fibrillation preoperatively and there was no change postoperatively.

All patients were taking digoxin at the time of preoperative assessment. Postoperatively, all but two patients were taking digoxin. No patient was taking a β-receptor blocking agent.

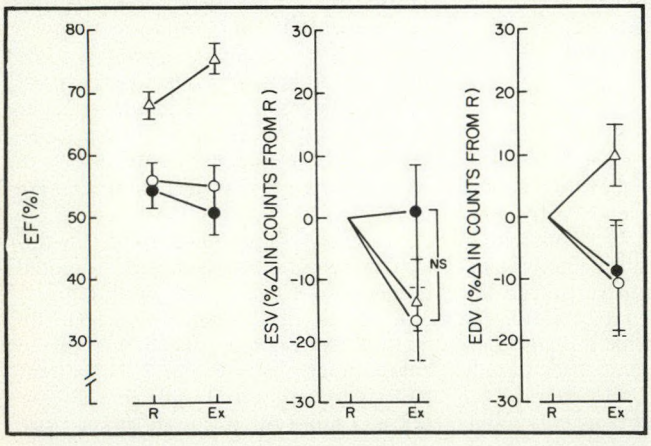

FIG. 1—Mitral stenosis. Rest (R) and exercise (Ex) left ventricular ejection fraction (EF) and percentage change (%△) in end-systolic volume (ESV) and end-diastolic volume (EDV) with exercise. Compared with normal (triangles) increase ($p < 0.001$), exercise EF failed to rise preoperatively (open circles) or postoperatively (closed circles) owing to decrease ($p < 0.01$) in exercise EDV. Values are mean ± standard error. NS = not significant.

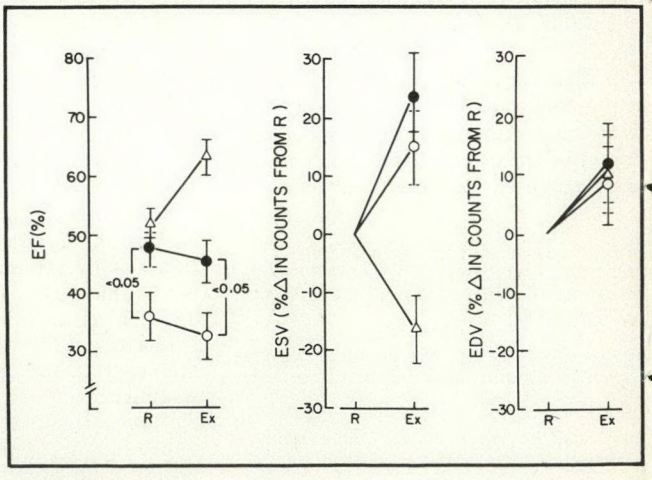

FIG. 2—Mitral stenosis. Rest and exercise right ventricular ejection fractions increased ($p < 0.05$) postoperatively (closed circles). Compared with normal (triangles) increase ($p < 0.001$), exercise EF failed to rise preoperatively (open circles) or postoperatively owing to increase ($p < 0.001$) in exercise ESV.

Group 1 (Figs. 1 and 2)

Preoperatively, all patients with mitral stenosis were in New York Heart Association class III for dyspnea or fatigue. At the time of follow-up, 11 patients were in class I and 2 in class II. Rest and exercise heart rate and systolic blood pressure were unchanged postoperatively from preoperative values (Table I). Changes from rest to exercise were significant ($p < 0.001$) and no differences occurred postoperatively.

The results for left and right ventricular function are set forth in Tables II and III respectively. The significant ($p < 0.001$) rise from rest to exercise of the left ventricular ejection fraction in healthy people did not occur in patients with mitral stenosis preoperatively or postoperatively, although three patients did have an increased ejection fraction postoperatively, at rest, while five had a substantial decrease (5% or more). Likewise, the significant ($p < 0.001$) rise in right ventricular ejection fraction from rest to exercise in healthy subjects did not occur in those with mitral stenosis.

None of the patients had evidence of mitral stenosis at follow-up.

Group 2 (Figs. 3 and 4)

All patients in this group were in New York Heart Association class III for dyspnea or fatigue preoperatively. At follow-up, five patients were class I and three were class II. Rest and exercise heart rates and systolic blood pressures postoperatively did not differ substantially from the preoperative values (Table I). All changes from rest to exercise were significant ($p < 0.001$).

Tables IV and V show the results of left and right ventricular function at rest and after exercise. As in group 1, there was no significant change in either left or right ventricular ejection fraction from rest to exercise pre- or postoperatively. Four patients had a decrease and three patients an increase in rest ejection fraction (5% or more).

Table I—Preoperative and Postoperative Heart Rate and Systolic Blood Pressure at Rest and Exercise in Groups 1 and 2*

	Heart rate, beats/min		Systolic blood pressure, mm Hg	
Group	Rest	Exercise	Rest	Exercise
Control	65 ± 11	129 ± 20	129 ± 16	198 ± 28
1, mitral stenosis				
Preop	78 ± 14	131 ± 36	114 ± 12	141 ± 17
Postop	76 ± 12	130 ± 42	117 ± 17	153 ± 24
2, mitral regurgitation				
Preop	85 ± 15	129 ± 30	124 ± 11	155 ± 27
Postop	80 ± 14	130 ± 31	137 ± 26	176 ± 24

*Values are mean ± standard deviation.

Table II—Group 1, Mitral Stenosis. Left Ventricular Function Pre- and Postoperatively

	Ejection fraction, %				End-systolic volume, %*		End-diastolic volume, %*		
	Rest		Exercise						
Control	67 ± 5	†	76 ± 6	‡	−16 ± 24	NS	+10 ± 18	†	§
Preop	56 ± 11	NS	55 ± 17	NS	−19 ± 24	NS	−11 ± 20	NS	
Postop	55 ± 15		52 ± 15		+ 2 ± 28		− 8 ± 10		

*Percentage change in volume with exercise from resting value.
†$p < 0.01$.
‡$p < 0.001$.
§$p < 0.05$.

Table III—Group 1, Mitral Stenosis. Right Ventricular Function Pre- and Postoperatively

	Ejection fraction, %				End-systolic volume, %*			End-diastolic volume, %*		
	Rest		Exercise							
Control	51 ± 8	†	64 ± 11	‡	−21 ± 28	‡	‡	+ 5 ± 19	NS	NS
Preop	37 ± 15	†	32 ± 15	†	+15 ± 30	NS		+ 9 ± 33	NS	
Postop	48 ± 10		45 ± 12		+24 ± 28			+12 ± 35		

*Percentage change in volume with exercise from resting value.
†$p < 0.05$.
‡$p < 0.001$.

Discussion

Left Ventricular Function

The etiology of the impaired response of the left ventricular ejection fraction in patients with mitral stenosis surprisingly remains controversial. Gash and associates[8] found that of five patients with a left ventricular ejection fraction of less than 50%, four had normal intrinsic muscle function. Reduced systolic function was the result of an increased afterload without adequate Frank–Starling compensation. In contrast, other studies have suggested that impaired muscle function, which may have been due to chronic rheumatic myocarditis, results in a reduction in ejection fraction.[2,6,9,14-17] Others[32,33] have suggested that the presence of right ventricular dysfunction may depress left ventricular function. Although the mechanism of left ventricular dysfunction at rest was not examined in this study, both systolic and diastolic left ventricular impairment could have contributed to the diminished ejection fraction. Lack of improvement postoperatively in the left ventricular ejection fraction at rest suggested that impaired diastolic filling from mitral valve stenosis was not the sole cause of the reduced ejection fraction. Due to chronic rheumatic fibrosis, preoperative systolic function may have been impaired and so contributed to the decreased ejection fraction at rest. It is possible that the ejection fraction was falsely depressed by the use of equilibrium radionuclide ventriculography in the presence of atrial fibrillation. But this is unlikely since the value of radionuclide ventriculography in this situation has been either documented or commended by others.[34,35]

By determining volume changes with mitral stenosis, we were able to assess ejection fraction responses to exercise in greater detail. Preoperatively, a significant decrease occurred in exercise end-diastolic volume. Coupled with a normal decrease in end-systolic volume, the left ventricular ejection fraction failed to rise, suggesting that impaired diastolic filling was responsible for the abnormal ejection fraction response to exercise. Since the heart rate did not increase beyond the normal exercise heart rate, reduced diastolic filling time was not responsible.

Postoperatively, impaired diastolic filling persisted. Moreover, there was a slight rise in end-systolic volume. Thus, mitral valve surgery did not improve exercise left ventricular function as measured by these parameters. Possibly, diastolic filling remained abnormal because of prosthetic valve narrowing, a consistent finding following mitral valve replacement.[36] In addition, the presence postoperatively of atrial fibrillation may have reduced end-diastolic filling. The slight rise in end-systolic volume indicates a reduction in exercise systolic function. This may have occurred during the perioperative period but more likely paradoxical septal motion contributed to this finding.[37]

In contrast to mitral stenosis, mitral regurgitation is associated with major hemodynamic left ventricular stress. The left ventricle compensates by several mechanisms. Wall thickness increases in relation to the increase in chamber size and the chamber becomes spherical.[22] Major increases in left ventricular and left atrial compliance permit a reduction in end-diastolic pressure.[18-22] The enlarged left atrium can accept very large volumes of blood at the onset of systole and in doing so, markedly reduces resistance to left ventricular outflow. These adaptive mechanisms permit mitral regurgitation to be present for prolonged periods without a reduction in left ventricular ejection fraction. In this study, a slight reduction in left ventricular ejection fraction postoperatively at rest and a significant decline in exercise ejection fraction suggest that mitral valve replacement may have been undertaken relatively late in the course of the disease. Normally, a decline in regurgitant volume combined with an increase in afterload (obstruction to the low impedance leak) results in a decrease in end-diastolic volume, little change in end-systolic volume and a slight fall in left ventricular ejection fraction. In the presence of preoperative left ventricular dysfunction, a greater fall in ejection fraction is likely after mitral valve replacement.[7,23-26]

Right Ventricular Function

In this study, the right ventricular ejection fraction preoperatively was depressed at rest with both mitral stenosis and regurgitation. Winzelberg and associates[38] noted a relation between pulmonary artery pressure and right ventricular ejection fraction in patients with aortic and mitral valve disease. The ejection fraction was decreased in over half the patients with right ventricular peak systolic pressures greater than 50 mm Hg. However, this decrease may not relate to a decline in intrinsic muscle function. Wroblewski and associates[39] found that in the presence of moderate pulmonary hypertension, removal of pulmonary artery pressure from the calculation of right ventricular performance showed that contractility was not impaired. Indeed, in patients with mitral stenosis, right ventricular ejection fraction improved postoperatively in the present study, probably owing to a reduction in pulmonary artery pressure.

During exercise, pulmonary artery pressure may increase further because increased forward flow is obstructed.[9] Thus, as our preoperative study demonstrated with mitral stenosis and

Table IV—Group 2, Mitral Regurgitation. Left Ventricular Function Pre- and Postoperatively

	Ejection fraction, %					
	Rest		Exercise		End-systolic volume, %*	End-diastolic volume, %*
Control	67 ± 5	†	76 ± 6	‡	−16 ± 24 NS	+10 ± 18 NS
Preop	54 ± 11	NS	57 ± 9	†	− 9 ± 19 † §	− 4 ± 20 NS NS
Postop	49 ± 12		46 ± 8		+11 ± 37	0 ± 25

*Percentage change in volume with exercise from resting value.
†$p < 0.05$.
‡$p < 0.001$.
§$p < 0.01$.

Table V—Group 2, Mitral Regurgitation. Right Ventricular Function Pre- and Postoperatively

	Ejection fraction, %					
	Rest		Exercise		End-systolic volume, %*	End-diastolic volume, %*
Control	51 ± 8	†	64 ± 11	‡	−21 ± 28 ‡	+ 5 ± 19 NS
Preop	30 ± 17	NS	24 ± 17	NS	+29 ± 14 NS ‡	+19 ± 8 NS NS
Postop	38 ± 15		31 ± 17		+39 ± 38	+19 ± 26

*Percentage change in volume with exercise from resting value.
†$p < 0.01$.
‡$p < 0.001$.

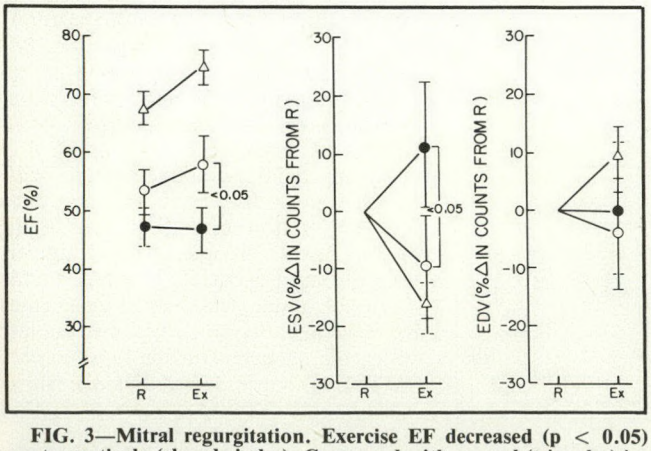

FIG. 3—Mitral regurgitation. Exercise EF decreased ($p < 0.05$) postoperatively (closed circles). Compared with normal (triangles) increase ($p < 0.001$), exercise EF failed to rise postoperatively owing to increase ($p < 0.01$) in exercise ESV. Open circles = preoperative values.

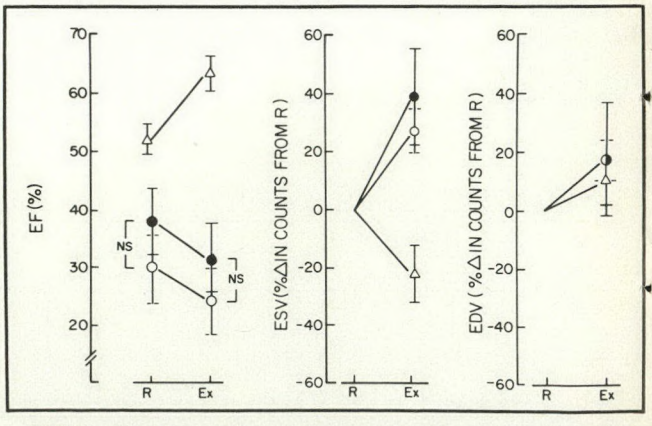

FIG. 4—Mitral regurgitation. Compared with normal (triangles) increase ($p < 0.001$), exercise EF failed to rise preoperatively (open circles) or postoperatively (closed circles) owing to increase ($p < 0.001$) in exercise ESV.

mitral regurgitation, exercise may be associated with an abnormal response of the right ventricular ejection fraction. Surprisingly, right ventricular ejection fraction also declined postoperatively. Although the exercise ejection fraction improved significantly in patients with mitral stenosis compared with the preoperative value, it failed to increase from the rest value because of a rise in end-systolic volume. Similarly, the exercise ejection fraction failed to rise from rest in patients with mitral regurgitation owing to an increase in end-systolic volume. These hemodynamic alterations, comparable in magnitude to those found preoperatively, implied depressed systolic function. Exercise systolic function may have been impaired postoperatively for several reasons. First, a significant gradient across the prosthetic mitral valve during exercise could cause an increase in right ventricular afterload. Although prosthetic valves vary in their flow gradients, a mild gradient usually exists.[36] Second, irreversible damage to the right ventricular myocardium may have occurred because of the hemodynamic stress of a chronically elevated pulmonary artery pressure. Improvement in contractility postoperatively would be unexpected. Third, tissue may have been damaged during the perioperative period. Conceivably, gradual improvement in myocardial function with an increase in ejection fraction could occur beyond our follow-up of 6 to 12 months.

In summary, left ventricular ejection fraction remained unchanged after operation for mitral stenosis but was reduced after operation for mitral regurgitation. Right ventricular function improved after operation for mitral stenosis; it remained unchanged after operation for mitral regurgitation.

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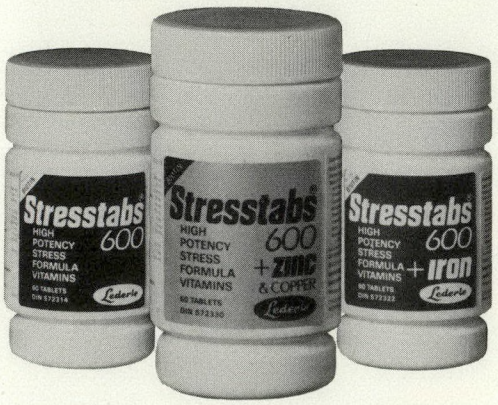

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G.W. HODGINS, MD;* J.W. DUTTON, MD, FRCS[C]†

Transluminal Dilatation for Takayasu's Arteritis

Takayasu's arteritis, pulseless disease or occlusive thromboaortopathy, is a progressive disease usually of young women. Early morbidity and death result from ischemia of vital organs. The results of surgical revascularization have been disappointing.

Two women with Takayasu's arteritis are reported. They underwent transluminal dilatation of serious symptomatic stenoses of the origins of the left carotid, left subclavian, renal and superior mesenteric arteries. Four repeat dilatations were required. There was one complication.

Clinical syndromes of transient cerebral ischemia, upper limb claudication, renal failure and intestinal angina have been reversed by transluminal dilatation.

Percutaneous transluminal dilatation is a suggested alternative to surgical revascularization in selected patients with Takayasu's arteritis.

L'artérite de Takayasu est une maladie qui se distingue par l'absence de pouls ou par l'oblitération de l'aorte et de ses branches. La maladie progressive affecte d'une manière prédominante les jeunes femmes. La morbidité précoce et la mort peuvent être les conséquences causées par l'ischémie des organes vitaux. Les résultats de la révascularisation chirurgicale ont été décourageants.

La dilatation des artères par la technique de l'entrée d'un catheter a été faite aux endroits où les symptômes de la sténose étaient les plus considérables, c'est-à-dire à l'origine de la carotide gauche, sous-clavière gauche, rénale et l'artère mésenterique supérieure. Le procédé a dû être répété quatre fois; une complication s'est présentée.

Les syndrômes médicaux des attaques transitoires de l'ischémie cérébrale, la claudication des extrémités supérieures, la défaillance rénale et l'angine intestinale ont été corrigées par la technique de la dilatation des artères.

Cette technique a été suggérée comme une alternative à la revascularisation chirurgicale chez les sujets choisis atteints de l'artérite de Takayasu.

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Takayasu's arteritis is a progressive inflammatory arteriopathy whose cause is unknown. It results in thickening of the arterial wall, leading to constriction or occlusion, occasionally aneurysmal dilatation and, rarely, thrombus formation in the aorta and its major branches.[1]

The clinical history of Takayasu's arteritis is often one of slow progression interspersed with acute morbid episodes due to inadequate blood supply to vital organs such as brain, kidneys or intestine.[2]

The success of percutaneous transluminal angioplasty as a new therapeutic modality for atherosclerotic obstructive disease has prompted its use for the treatment of Takayasu's arteritis. This report is to update our experience[3] and document further expansion of the technique to include stenoses of the renal[4] and superior mesenteric artery origins involved in Takayasu's arteritis.

Case Reports

Case 1

A 34-year-old woman had a history of severe left-sided headaches, episodes of blindness of the left eye lasting up to 3 minutes, vertigo and weakness of the left arm manifested by an inability to hang up cups or wash dishes.

No blood pressure could be recorded in the left arm, which was markedly cooler than the right and showed slow capillary filling. Bruits were heard over the entire anterior precordium including the left infraclavicular region.

Arch aortography demonstrated typical findings of Takayasu's arteritis with severe stenoses at the origins of the left common carotid and subclavian arteries (Fig. 1). There was retrograde filling of the left vertebral artery in later phases of the injection.

Transluminal dilatation was undertaken. A guide wire was passed across the left subclavian ostial stenoses and a no. 7 French dilatation catheter with a balloon 6 mm in diameter was advanced over it. Four balloon inflations were accomplished without complication. Following dilatation, there was marked improvement in the left arm pulse and diminution of the systolic gradient across the stenosis from 90 mm Hg to 10 mm Hg. Postdilatation aortography showed angiographic improvement as well as antegrade opacification of the left vertebral artery.

Over the next 2 days, the patient experienced quite marked hyperesthesia of the left arm, thought to be due to the increased blood flow to that arm.

Eight days later a retrograde left carotid angioplasty was performed through a left common carotid arteriotomy. A no. 7 French Gruntzig balloon catheter with guide was inserted through the arteriotomy and advanced under fluoroscopic control across the left common carotid ostial stenosis. Three dilatations were performed. Following each deflation of the balloon, blood was allowed through the arteriotomy. No embolic debris was seen. An increase in systolic pressure of 40 mm Hg was recorded distally after dilatation.

Intraoperative arteriography showed satisfactory dilatation. The patient recovered without complication.

Fifteen months later, repeat arteriography showed increased stenosis of the origins of the left subclavian (gradient 60 mm Hg) and left carotid (gradient 65 mm Hg) arteries. Repeat percutaneous transluminal dilatation was performed. Gradients were reduced to 25 mm Hg at the origin of the left subclavian artery and 20 mm Hg at the origin of the left carotid

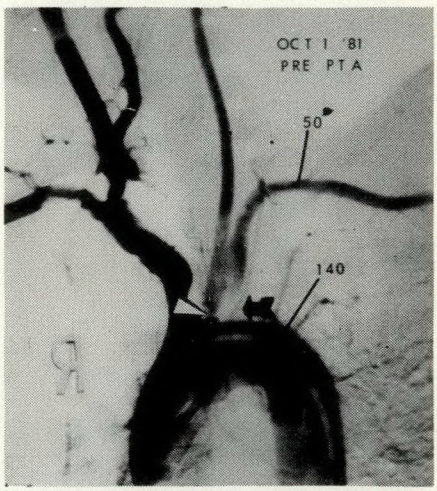

FIG. 1—Case 1. Arch aortogram demonstrates stenoses at origins of left subclavian and left carotid arteries (arrows). Systolic pressures were 140 mm Hg proximally and 50 mm Hg distally.

Table I—Case 1. Systolic Pressure Gradients (mm Hg) before and after Percutaneous* Transluminal Angioplasty

	Date of angioplasty								
	Oct. 1981		Feb. 1983		Apr. 1983		June 1983		
Pressure gradient	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Sept. 83
Aorta to left carotid artery	80	40*	65	20	–	–	–	–	20
Aorta to left subclavian artery	90	10	60	25	–	–	–	–	10
Aorta to superior mesenteric artery	–	–	–	–	130	75	105	35	30

*First dilatation through left common carotid arteriotomy.

artery. Repeat pressure studies done 6 months later demonstrated no change in the degree of stenosis (Table I) (Fig. 2).

During the patient's period of observation, she began to complain of postprandial midabdominal colicky pain. No diarrhea or weight loss was noted. The only new physical finding was a loud midabdominal bruit.

Biplane arteriography documented a complex stenosis of the celiac axis not suitable for dilatation. A severe stenosis of the superior mesenteric artery (gradient 130 mm Hg) was found (Fig. 3). Transluminal dilatation of this vessel was accomplished successfully to a residual gradient of 75 mm Hg.

Symptoms and increased stenosis (gradient 105 mm Hg) of the superior mesenteric artery occurred within 3 months. Repeat transluminal dilatation reduced the gradient to 35 mm Hg (Fig. 4). This gradient has remained stable for 6 months (Table I).

Case 2

A 34-year-old woman was admitted with severe nausea, vomiting and azotemia. Her serum creatinine level was 707 μmol/L.

Twelve years previously, she had been investigated for severe hypertension, and Takayasu's arteritis type II (Kimoto variety) had been diagnosed.[5] Aortography documented severe left renal ostial stenosis, celiac and superior mesenteric artery occlusions and stenosis of the left common iliac artery. Aortorenal and aortosuperior mesenteric artery bypasses were performed. The renal bypass failed early and left nephrectomy was done to control recurrent hypertension.

Repeat aortography 3 years later documented occlusion of the superior mesenteric artery graft and 95% ostial stenosis of the remaining right renal artery. Further surgery was not considered because the previous grafts had failed to remain patent. Hypertension recurred and was difficult to control despite aggressive medical management.

Renal failure occurred 8 years later, resulting in the present admission. Rehydration and temporary transvenous dialysis were undertaken. She remained anuric. Angiography documented a 161 mm Hg gradient (165/90–4/4 mm Hg) across the ostial stenosis of the right renal artery (Fig. 5). Retrograde transluminal dilatation using a no. 7 French Gruntzig catheter successfully reduced the arterial gradient to 45 mm Hg (Fig. 6). Urine production resumed and the serum creatinine level stabilized at 159.6 μmol/L.

Over a 9-month period, hypertension became severe and repeat aortography documented recurrent stenosis with a gradient of 170 mm Hg. A repeat dilatation was only partially successful. A 95 mm Hg gradient remained and dissection of the distal renal artery was seen. Over the next 48 hours renal failure recurred. Repeat aortography documented a thrombus in the right renal artery. Streptokinase therapy at 15 000 U/h was given. Dissolution did not result and the clot was thought to be subintimal. Repeat dilatation of the area of the subintimal hemorrhage successfully re-established adequate renal blood flow (resulting in a residual gradient of 60 mm Hg) and renal function returned. Her serum creatinine level remained stable at 159.6 to 212 μmol/L over an 8-month period but her hypertension persisted.

Discussion

The course of the individual afflicted with Takayasu's arteritis is difficult to predict. An initial delay in diagnosis is common.[2] Of those with documented

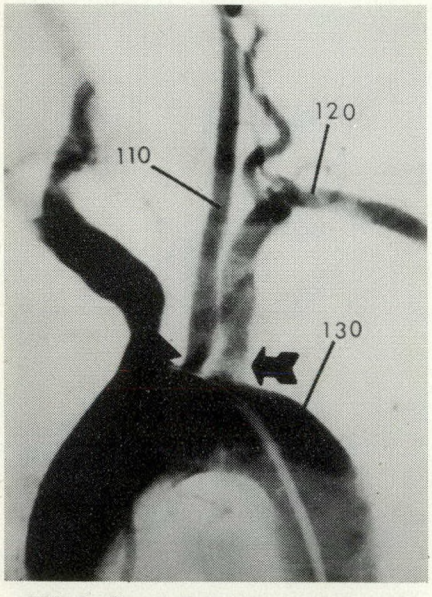

FIG. 2—Case 1. Follow-up aortogram after 15 months. Origins of left subclavian and left carotid arteries well dilated. 110, 120, 130 = systolic blood pressures in mm Hg.

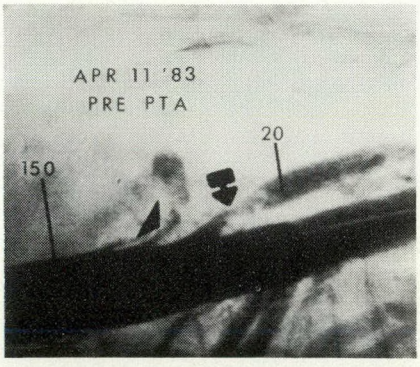

FIG. 3—Case 1. Lateral abdominal aortogram shows stenosis of celiac axis (left arrow) and superior mesenteric artery (right arrow). Numbers indicate systolic pressures in mm Hg proximally and distally to superior mesenteric artery stenosis. Gradient is 130 mm Hg.

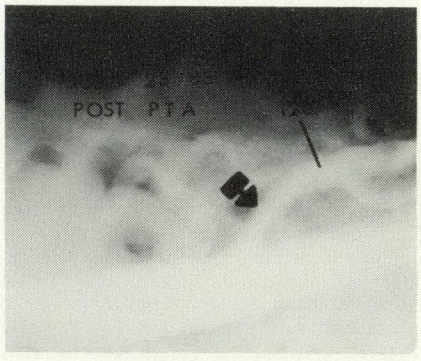

FIG. 4—Case 1. Lateral aortogram following second transluminal dilatation. Arrow = site of previous stenosis of superior mesenteric artery; 120 is systolic pressure in mm Hg distal to previous stenosis.

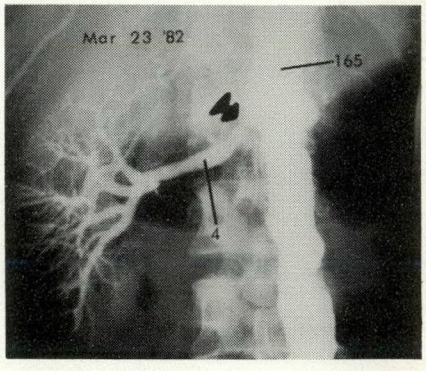

FIG. 5—Case 2. Abdominal aortogram. Arrow shows ostial stenosis of right renal artery. Systolic blood pressures are 165 mm Hg proximal and 4 mm Hg distal to stenosis.

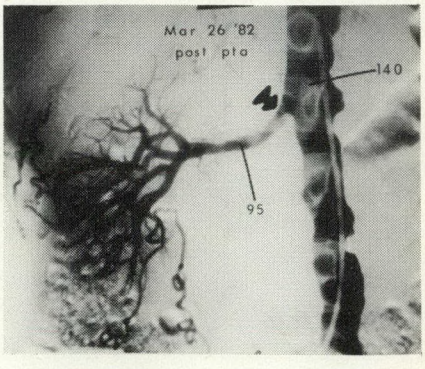

FIG. 6—Case 2. Abdominal aortogram following successful transluminal angioplasty of right renal artery. Systolic pressure gradient is now 45 mm Hg.

disease, morbidity is usually related to unrelieved renovascular hypertension, or visual and cerebral events thought to be secondary to ischemic episodes.

Medical therapy, particularly during the active phase of the disease, is directed towards preventing progression of the underlying inflammatory process of the arterial wall.

Revascularization is undertaken to prevent ischemic damage to end organs whose arterial supply is severely compromised by the disease, or to correct renovascular hypertension.

Surgical revascularization, however, has a higher morbidity and mortality in Takayasu's arteritis than in equivalent obstructive arteriopathy due to atherosclerosis.[6,7] In a review of the literature by Ishikawa,[6] 26.9% of the surgically treated patients died. Lupi-Herrera and associates[8] reported that four of five aortorenal grafts occluded in patients with Takayasu's arteritis and they have abandoned the procedure. Graft occlusion or anastomotic failure is thought to be related to active disease at the site of arterial anastomosis.

The use of percutaneous transluminal dilatation as the initial form of revascularization in Takayasu's arteritis has been reported.[9]

During our first attempt at dilatation at the origin of the left carotid artery, we used left common carotid arteriotomy through the neck[10] to prevent embolization. Cerebral blood flow was interrupted at the time of dilatation and blood and possible embolic debris were allowed through the arteriotomy. No debris was seen. As a result, subsequent percutaneous transluminal dilatation was performed using the femoral approach.

Castaneda-Zuniga and associates[4] have stressed the need to repeat transluminal dilatation should clinical signs or follow-up angiography document recurrent stenosis. Our experience with two patients requiring nine dilatations of four major vascular lesions supports the efficacy of repeated dilatation should it be required. Close follow-up, including the use of the noninvasive techniques and repeat angiography, have been useful in documenting recurrent stenosis before end-organ ischemia occurs.

While the long-term results of this form of therapy remain uncertain, percutaneous transluminal angioplasty appears to be a safe and logical initial technique for revascularizing severely stenotic arteries in patients with Takayasu's arteritis.

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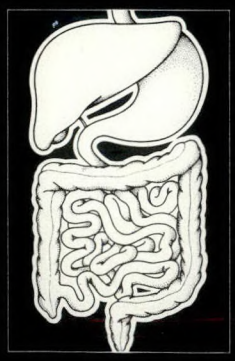

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Percutaneous Transluminal Angioplasty of Iliac Arteries: the Importance of Functional Studies

Results of percutaneous transluminal angioplasty of 60 iliac arteries are presented, with a follow-up of 3 to 12 months. The patency rate at 1 year was 95% using the thigh–brachial index as the criterion and 86% with the ankle–brachial index. Study of the patients with an exercise test component improved the sensitivity of the evaluation, demonstrating that both indices tend to underestimate the functional improvement. The authors propose a simple, cost-effective way for practitioners to follow-up their patients after percutaneous transluminal angioplasty.

Les auteurs présentent une série de 60 angioplasties transluminales percutanées de l'artère iliaque avec une post-observation de 3 à 12 mois. Le taux de succès à 1 an est 95% en utilisant l'index cuisse–bras comme critère et 86% avec l'index cheville–bras. En plus de ces mesures au repos, ils ont inclus une composante fonctionnelle dans l'évaluation par le laboratoire vasculaire et ont ainsi amélioré la sensibilité de leurs évaluation, démontrant que les indices ont tendance à sous-estimer l'amélioration après la dilatation par angioplastie. Les auteurs proposent aux praticiens une méthode simple et peu coûteuse de suivre leurs patients après angioplastie percutanée.

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The introduction of noninvasive vascular testing has made it possible to document accurately the natural history of disease and to assess and compare the results of treatment.[1] In many centres, noninvasive evaluation has now become an essential component of the clinical assessment of patients with known or suspected vascular disease before and after treatment.[2] We have followed up a group of patients with iliac artery disease before and after percutaneous transluminal angioplasty by measuring their performance at rest and after exercise with resting segmental pressure studies and functional evaluation. These studies were used to document the success of angioplasty, comparing the results of resting segmental studies with the functional evaluation during the follow-up period.

Patients and Methods

From October 1980 to April 1983, 142 percutaneous transluminal angioplasties were performed in our institution. Eighty-one involved the iliac arteries; in 60 of these the patients were followed up for 3 to 12 months and are included in this study. All angioplasties were performed by the same radiologist (M.H.) and evaluated by the same vascular laboratory technician (D.L.). All lesions were segmental (less than 4 cm long) and incompletely occluded.[3]

The following angioplasty technique was used: after local intradermal anesthesia with lidocaine 2%, a percutaneous puncture ipsilateral to the stenosis was performed at the level of the common femoral artery (few patients underwent contralateral puncture) and catheterization was carried out through the stenosis, using a leading guide wire. A balloon-tip catheter was then inserted over the guide wire (the balloon size was chosen according to the vessel diameter measured directly on the angiogram) and the ballon was manually inflated with a 10-mL syringe filled with Renografin-30. The balloon was inflated to full capacity and the dilatation repeated as necessary to increase the vessel diameter to normal size. Before inflation of the balloon, 5000 U of heparin were injected through the catheter. After removing the catheter and applying hand pressure, we applied a pressure dressing. All patients were nursed flat in bed overnight.

Evaluations were made before angioplasty, on the following day and at 3 and 12 months after. Each assessment included measurements of the ankle–brachial pressure index before and after exercise and the thigh–brachial pressure index, and an exercise tolerance test. The exercise tolerance test consisted of the walking time performance on a treadmill set at 2.4 kph with a 10° grade.[4] The exercise test was concluded after 5 minutes of walking or at the appearance of claudication when the time was noted and the ankle–brachial pressure measured. The walking distance is calculated by multiplying the walking time by the treadmill speed.

To assess the reproducibility of our results, the mean contralateral ankle–brachial pressure index was calculated before and after angioplasty. No signifi-

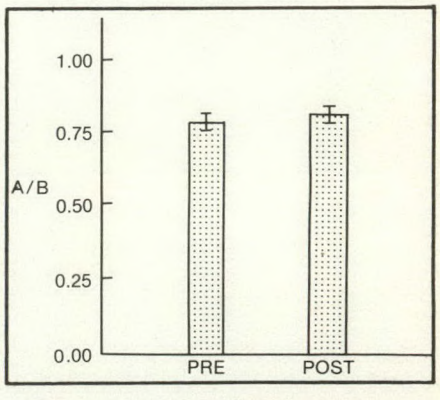

FIG. 1—Mean (± SEM) ankle–brachial pressure index (A/B) before and after angioplasty in contralateral limb.

cant difference was found ($p > 0.05$, Student's *t*-test), indicating that our method of measuring the indices is reliable (Fig. 1).

We define patency as any improvement over the preangioplasty index; our patency rates at 1 year were 95% (thigh–brachial) and 86% (ankle–brachial).

Results

Table I represents the group's performance in terms of indices. The results of the exercise tolerance test are expressed in Table II. To compare the sensitivity of each category of measurements, we expressed our data as percent improvement (Figs. 2 and 3).

Improvement after Angioplasty

Immediately after angioplasty (Fig. 2).—There was no significant difference between the improvement in the ankle–brachial pressure index and that for the thigh–brachial index. However, the differences in improvement between the ankle–brachial index and exercise tolerance and between the thigh–brachial index and exercise tolerance were significant ($p < 0.001$). There was no significant difference between the postexercise ankle–brachial index and the exercise tolerance test results.

Three months after angioplasty (Fig. 3).—This group includes 60 procedures; 55 patients were tested and 5 were lost to follow-up. There was a significant ($p < 0.01$) difference after angioplasty between the improvement in the ankle–brachial pressure index and in exercise tolerance and the thigh–brachial index and exercise tolerance. As before, improvement of the postexercise ankle–brachial index and exercise tolerance did not differ significantly.

Twelve months after angioplasty (Fig. 4).—In this group, 37 procedures were performed; 23 patients had examinations and 14 were lost to follow-up. There was a significant difference between the improvement in the thigh–brachial index and exercise tolerance ($p < 0.05$) and in the thigh–brachial index and postexercise ankle–brachial index ($p < 0.01$), as well as in the pre- and postexercise ankle–brachial indices ($p < 0.02$). However, there was no significant difference between the ankle–brachial pressure index and the results of the exercise tolerance test ($0.1 > p > 0.05$).

Using the vascular laboratory data and the recurrence of symptoms as criteria, we had eight failures in our series of common iliac artery angioplasties. One procedure involved a dilatation of a distal anastomosis of an aortoiliac graft (the only procedure on a graft in our series). Three were performed on patients with disease of the superficial femoral artery and tibial artery, two on patients with tibial artery disease alone and two patients with no distal disease. Looking at the successful group, 1 year after angioplasty, we found that all but one had two- or three-vessel run-off.

Discussion

Our patency rates (95% with thigh–

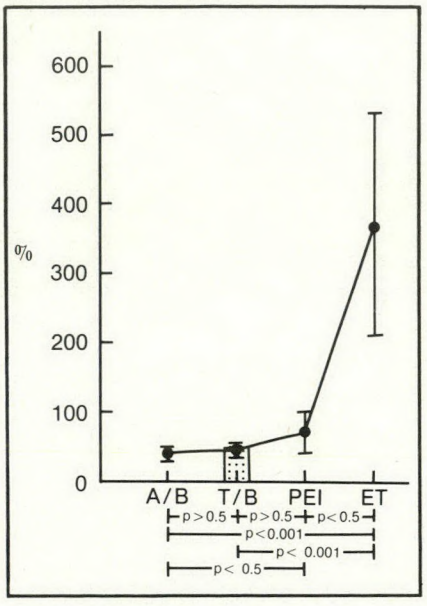

FIG. 2—Mean (± SEM) percent improvement of indices after angioplasty. A/B = ankle–brachial pressure index, T/B = thigh–brachial pressure index, PEI = postexercise ankle–brachial pressure index, ET = exercise tolerance test.

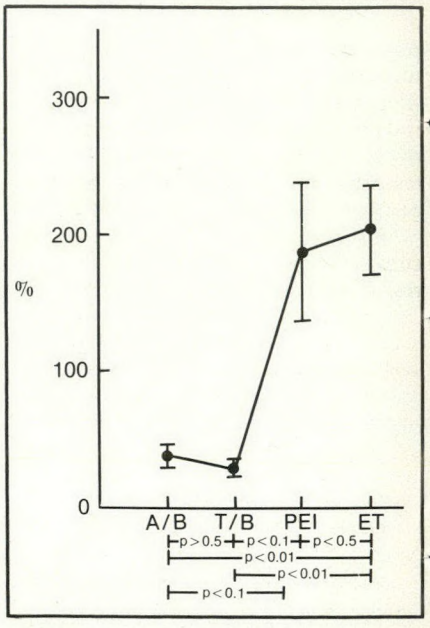

FIG. 3—Mean (± SEM) percent improvement of indices at 3 months after angioplasty.

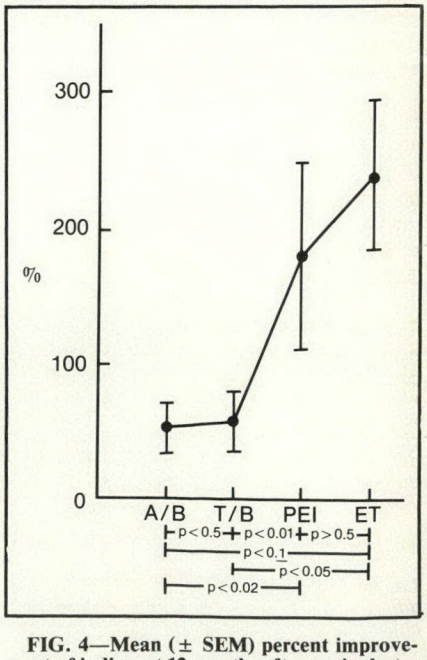

FIG. 4—Mean (± SEM) percent improvement of indices at 12 months after angioplasty.

Table I—Indices before and after Percutaneous Transluminal Angioplasty*

Index	Before angioplasty	Day after angioplasty	3 mo	12 mo
Ankle–brachial pressure	0.56 ± 0.02	0.73 ± 0.03†	0.78 ± 0.02†	0.82 ± 0.03†
Thigh–brachial pressure	0.62 ± 0.02	0.83 ± 0.02†	0.83 ± 0.02†	0.87 ± 0.14†
Postexercise ankle–brachial pressure	0.43 ± 0.04	0.62 ± 0.09‡	0.79 ± 0.03†	0.78 ± 0.05†

*Figures are mean ± standard error.
†$p < 0.001$.
‡$p = 0.05$.

Table II—Exercise Tolerance Test: Improvement before and after Angioplasty*

Exercise	Before angioplasty	Day after angioplasty	3 mo	12 mo
Time, min	1.72 ± 0.22	2.83 ± 0.58†	3.90 ± 0.25‡	4.33 ± 0.20‡
Distance, m	45.3 ± 5.7	74.7 ± 15.3	102.9 ± 6.6	114.3 ± 5.1

*Figures are mean ± standard error.
†$p < 0.05$.
‡$p < 0.001$.

brachial and 86% with ankle-brachial pressure measurements) were comparable to those noted by Neiman and associates[5] in their review of more than 4000 cases of peripheral vascular disease treated by percutaneous transluminal angioplasty. We found no significant difference between the improvement in ankle-brachial and thigh-brachial indices immediately after angioplasty, probably because most of our patients had two- and three-vessel run-off in the calf. Incorporating an exercise tolerance test increased the sensitivity of our evaluation, indicating that thigh-brachial and ankle-brachial pressure measurements tend to underestimate the functional improvement in these patients. This is also true at 3 months; however, at 12 months, the difference between the ankle-brachial pressure index and results of the exercise tolerance test was not statistically significant ($0.1 > p > 0.05$). We think that this is due to a smaller sample number (23 procedures). Still, the exercise tolerance test seems to be a more sensitive indicator of patient performance.

Our early results suggest that percutaneous transluminal angioplasty offers results comparable to those of aortoiliac bypass grafting[6] if patients are carefully selected.[3,7-10] None of our patients had complete obstruction and all lesions involved short segments (less than 4 cm). Four of the eight failures had severe distal disease, including occlusion of the superficial femoral artery and poor run-off. One patient had a distal graft dilated. Only one successful patient had poor run-off in the calf, emphasizing the importance of patient selection for angioplasty. As noted in 1975 by Malone and associates[6] in the case of aortofemoral bypass grafting, the postoperative symptoms of patients after angioplasty correlate well with patency.

Conclusions

This study indicates that with proper patient selection and technique, transluminal angioplasty of the iliac arteries is an effective treatment, with patency rates comparable to those of bypass procedures. The inclusion of a functional component in follow-up evaluations more closely mimics clinical conditions and is more sensitive than resting studies alone. Thus, the referring doctor can successfully follow up patients after angioplasty by noting the walking distance and time before the onset of claudication in addition to routine physical examination. Deterioration of symptoms or signs is an indication for vascular laboratory testing and, if necessary, angiographic reappraisal.

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Étude comparative des angioplasties transluminales percutanées iliaques et fémoro-poplitées dans l'artériopathie des membres inférieurs

À la lumière d'une série de 100 angioplasties transluminales percutanées (ATP) consécutives, les auteurs comparent les données anatomo-radiologiques et les résultats immédiats et tardifs en fonction de l'étage lésionnel iliaque et fémoro-poplité. À l'étage sus-crural 57 ATP concernent l'iliaque primitive (36) et l'iliaque externe (21). À l'étage sous-crural 43 ATP concernent l'artère poplitée haute (9) et l'artère fémorale superficielle (34). L'ATP de la lésion iliaque primitive est dominante avant l'âge de 60 ans par rapport à l'ATP fémoro-poplitée ($p < 0.05$). À l'étage iliaque 89% des patients ont un stade de claudication sévère; à l'étage fémoro-poplité les troubles trophiques sont retrouvés dans 39% des cas. Le caractère "dominant" ou "accessoire" de la lésion n'intervient pas de façon différente dans l'indication selon le niveau. La thrombose segmentaire reperméabilisée représente 44.2% des indications d'ATP fémoro-poplité contre 7% à l'étage iliaque ($p < 0.04$). Le taux d'échec est moindre à l'étage iliaque que fémoro-poplité. La surveillance des suites thérapeutiques concerne 86.6% des patients avec un recul de 22 mois en moyenne. Les indices systoliques de la cuisse après ATP iliaque et de la cheville après ATP fémoro-poplité sont majorés de façon significative ($p < 0.01$). À l'étage fémoro-poplité, dans 74% des cas, le patient est totalement asymptomatique. Un seul échec est noté (3.8%); amputation de cuisse au 12e mois après ATP. À l'étage iliaque, dans 91% des cas, une amélioration est observée et 70% des patients sont asymptomatiques. Globalement, le taux de succès (perméabilité et amélioration clinique) actuariel est de 92% ± 0.09%.

The authors compared the anatomo-radiologic data from a series of 100 consecutive percutaneous transluminal angioplasties (PTA), as well as the im-

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mediate and long-term results as a function of the level of the lesion — iliac or femoropopliteal. Proximal to the thigh, there were 57 PTAs, 36 of the common iliac and 21 of the external iliac. In the lower thigh, there were 43 PTAs, 9 of the upper part of the popliteal artery and 34 of the external femoral artery. Percutaneous transluminal angioplasty of the common iliac lesion was dominant in patients under 60 years of age ($p < 0.05$). At the iliac level, 89% of the patients had severe claudication; at the femoropopliteal level, 39% had trophic problems. The "dominant" or "accessory" character of the lesion did not modify the indication for the procedure, regardless of the level. Segmental thrombosis accounted for 44.2% of the femoropopliteal PTA indications, compared with 7% at the iliac level ($p < 0.04$). The failure rate was less at the iliac than at the femoropopliteal level. Follow-up was available for 86.6% of the patients for an average of 22 months. The systolic indices at the thigh after iliac PTA and at the ankle after femoropopliteal PTA were significantly increased ($p < 0.01$). At the femoropopliteal level, 74% of the patients were totally asymptomatic. There was one failure (3.8%); amputation at thigh level was carried out 12 months after the PTA. At the iliac level, improvement was observed in 91% of the patients and 70% became asymptomatic. The overall success rate (clinical patency and improvement) was 92% ± 0.09%, based on the life-table method.

Depuis le rapport préliminaire sur l'angioplastie transluminale percutanée (APT) de Dotter et Judkins,[1] cette technique, standardisée par Gruntzig et Hopff[2] et Gruntzig et Kumpe,[3] peut être considérée comme l'une des plus importantes acquisitions de l'angiographie thérapeutique. Élégante car peu agressive, elle permet sans geste chirurgical direct une recanalisation ou dilatation des thromboses et sténoses artérielles segmentaires; l'élargissement endoluminal est le fruit d'une fragmentation avec clivage de la plaque athéromateuse intimale, la média et l'adventice se laissant distendre du fait de leur élasticité.[4] Nous mettons en corrélation les indications anatomocliniques et les résultats des ATP à l'étage sus-crural et fémoro-poplité.

Étude de la série

De 1979 à 1983 nous avons étudié 100 ATP consécutives. C'est après un bilan fonctionnel clinique, des explorations vasculaires débimétriques non pénétrantes et une analyse des lésions radiologiques que les indications des ATP ont été posées au terme de réunions conjointes entre médecins angiologiques, radiologues et chirurgiens vasculaires. Les ATP ont été réalisées par les radiologues vasculaires. Les comparaisons statistiques ont utilisé les tests du chi carré, de l'écart type, du *t* de Student ainsi que les calculs actuariels de succès.

Répartition topographiques des ATP

À l'étage sous-crural 43 ATP se répartissent en deux groupes — 9 ATP poplités hautes et 34 ATP de l'artère fémorale superficielle. Nous n'avons pas posé d'indication d'ATP des artères fémorales profondes ou poplitées basses.

À l'étage sus-crural 57 ATP se répartissent en 36 cas concernant l'artère iliaque primitive et 21 cas de l'artère iliaque externe. Nous n'avons pas retrouvé de cas d'ATP de l'hypogastrique.

Âge et sexe des patients (fig. 1)

Reflet de l'épidémiologie de la maladie athéroscléreuse, la prépondérance des ATP est au sexe masculin (3:1). La femme est touchée par l'athérome, et par conséquent justiciable d'ATP, à un âge significativement plus élevé que l'homme (69 ans contre 58.4 années en moyenne). La comparaison du niveau de l'ATP en fonction de l'âge des patients (tableau I) montre qu'au delà de 60 ans, l'ATP fémoro-poplitée est le plus fréquemment rencontrée. L'axe de l'artère iliaque externe est concerné de façon identique quelle que soit l'âge; par contre l'ATP d'une lésion cible de l'artère iliaque primitive est dominante avant 60 ans ($p < 0.001$).

Stade clinique

Globalement, 74% des patients sont au stade de claudication intermittente sévère et 3% des patients ont une lésion asymptomatique dilatée en complément de lésions plus importantes. Les ATP pour sauvetage de membre concernent 23% des cas: douleurs de décubitus (15%) ou troubles trophiques (8%). La corrélation des stades cliniques en fonction du niveau de l'ATP (tableau II) montre qu'à l'étage

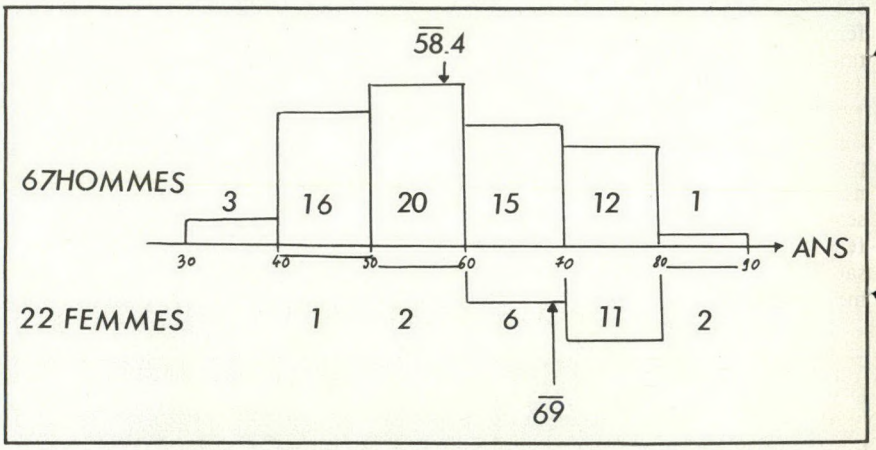

FIG. 1—Répartition des patients en fonction de leur âge et sexe.

Tableau I—Niveau de l'ATP et âge

Niveau	Âge, ans < 60	Âge, ans > 60	Total
ATP fémoropoplitée	7	33	40
ATP iliaque externe	9	8	17
ATP iliaque primitive	26	6	32
Total	42	47	89

$\chi^2 = 29.26$, degrés de liberté = 2, $p < 0.01$.

Tableau II—Niveau de l'ATP et stade clinique

Stade clinique	Niveau: Iliaque	Niveau: Fémoro-poplité	Total
Troubles trophiques ou douleurs de décubitus	6	17	23
Claudication intermittente	51	26	77
Total	57	43	100

Écart réduit = 3.4, $p < 0.001$.

iliaque, dans 89% des cas (51 sur 57), l'indication est motivée par un stade de claudication intermittente sévère. Par contre, dans 11% (6 sur 57) seulement des cas, il existe un stade de sauvetage de membre. À l'étage fémoro-poplité on constate une dominance significative ($p < 0.001$) de l'indication de l'ATP pour sauvetage (39.5%) (17 sur 43) par rapport à l'ATP iliaque.

Résultats

Lésions anatomiques

La lésion cible concernée par l'ATP peut s'intégrer dans un tableau d'atteinte étagée polysténosante; elle est alors accessoire (38%) ou bien dominante, déterminante dans la symptomatologie fonctionnelle (59%). Dans ce dernier cas l'ATP se veut curative. Il apparaît que ce caractère "accessoire" ou "dominant" n'intervient pas dans l'indication selon le niveau sus- ou sous-crural; la lésion est déterminante dans 64.3% (27 sur 42) des ATP fémoro-poplitées et dans 58.2% (32 sur 55) des ATP iliaques. À l'étage fémoro-poplité, les thromboses segmentaires à reperméabiliser représentent 44.2% (19 sur 43) des indications contre 7% (4 sur 57) à l'étage iliaque ($p < 0.04$); l'indication des ATP sus-crurales est dans plus de 9 cas sur 10 une sténose. Ces données anatomiques correspondent à l'observation faite cliniquement de lésions fémoro-poplitées dilatées à un stade de sauvetage de membre. La longueur moyenne des thromboses reperméabilisées est de 3.5 ± 2.5 cm (écart type) et celles des sténoses de 1.8 ± 1.5 cm. La longueur moyenne de la thrombose est significativement plus importante que celle de la sténose ($p < 0.01$). Il n'existe pas de différence significative entre les longueurs moyennes des thromboses reperméabilisées selon le niveau sus- ou sous-crural de même qu'entre les sténoses à ces niveaux.

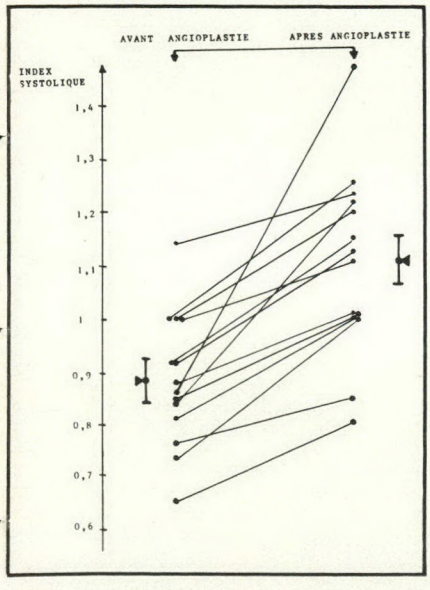

FIG. 2—Évaluation hémodynamique des 14 ATP iliaques (indice systolique à la cuisse). Recul moyen de 13.3 mois (extrêmes: 1 à 28 mois). Écart type de la moyenne. Différence moyenne ($\overline{\Delta}$) = 0.223 ± 0.14, t de Student (t) = 5.9, degrés de liberté (ddl) = 13, $p < 0.001$.

Résultats immédiats des ATP selon le niveau sus- ou sous-crural

Le taux d'échec radio-clinique lié à la méthode est de 18% (18 sur 100); la comparaison des échecs radio-cliniques selon le niveau iliaque (14%) (8 sur 59) et fémoro-poplité (23%) (10 sur 43) est en faveur d'un moindre taux à l'étage iliaque à la limite de la signification statistique ($p < 0.06$). L'analyse des 10 échecs d'ATP sous-crurales montre que sur huit lésions de l'artère fémorale superficielle la lésion n'a pu être franchie dans cinq cas (quatre thromboses segmentaires et une sténose pré-occlusive); dans les trois autres cas, la dilatation n'a pas été suffisante (absence d'amélioration clinique dans un cas et thrombose secondaires dans les autres suivies d'une amputation de cuisse pour l'une et d'une sympathectomie lombaire pour l'autre). Les deux échecs d'ATP poplitée pour des lésions pré-occlusives et thrombotiques ont entraîné une amputation et une sympathectomie lombaire.

Au niveau sus-crural, les échecs (huit cas) sont le fait de lésions non franchies, pré-occlusives deux fois et non dilatables trois fois. Dans trois cas, malgré une dilatation radiologique correcte de lésions "accessoires", il existe un échec clinique. La morbidité liée à l'abord percutané fémoral est la même quelque soit le niveau de l'ATP: sept hématomes au point de ponction, non chirurgicaux.

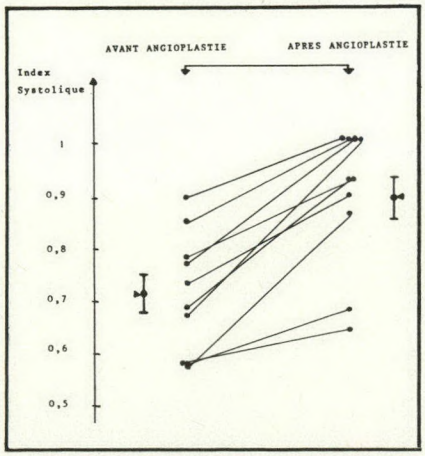

FIG. 3—Évaluation hémodynamique des 10 ATP fémoro-poplitées (indice systolique jambier). Recul moyen de 12 mois (extrêmes: 1 à 30 mois). $\overline{\Delta}$ = 0.191 ± 0.09, (t) = 6.6, ddl = 9, $p < 0.001$.

Résultats tardifs comparés entre ATP iliaques et fémorales

La surveillance des suites thérapeutiques, d'une durée moyenne de 22 mois (3 à 38 mois), concerne 86.6% des ATP réussies. Les indices systoliques à la cuisse après ATP iliaque sont significativement majorés: l'indice moyen avant ATP, de 0.88% ± 0.03%, est augmenté à 1.1% ± 0.04% ($p < 0.001$). Les mêmes constatations sont faites au niveau de la cheville après ATP fémoro-poplitée: de 0.71% ± 0.03% l'indice passe à 0.90% ± 0.04% ($p < 0.001$) (figs. 2 et 3).

Sur le plan fonctionnel à l'étage fémoro-poplité, sur 27 ATP suivies, une amélioration est acquise dans 96.3% (26 sur 27) des cas et, dans 74% (20 sur 27) des cas, le patient est totalement asymptomatique (fig. 4a). Le cas d'amputation de cuisse observé (3.8%) a été secondaire à une gangrène que l'ATP a stabilisé pendant 12 mois. La lésion était pré-occlusive et "accessoire".

À l'étage iliaque, 44 patients soumis à une ATP ont été suivis. Dans 70% (31 sur 44) des cas, les patients sont asymptomatiques et dans 91% (40 sur 44) des cas une amélioration est observée. Quatre patients ont été opérés pour sténose récidivante, soit sur la zone antérieurement dilatée (trois fois à 10 et 12 mois), soit dans un segment artériel sus-jacent à l'ATP (fig. 4b).

Globalement, sur 71 patients suivis après ATP, le taux de succès actuariel (asymptomatique ou périmètre de marche augmenté) à 3 ans est de 92% ± 0.09%.

Discussion

Sur un plan technique, l'ATP a toujours été réalisée sous héparinate de sodium intraveineux. L'anticoagulation a

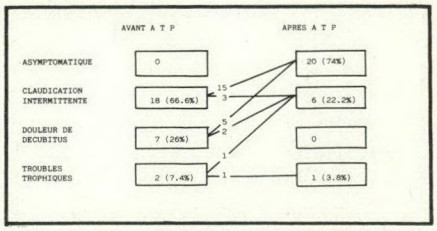

Fig. 4a

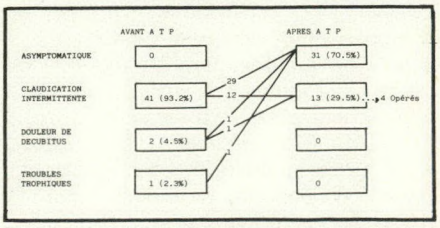

Fig. 4b

FIG. 4—Comparaison des résultats fonctionnels tardifs selon le niveau de l'ATP. (a) 27 fémoro-poplitée suivies, (b) 44 iliaques suivies.

été poursuivie pendant 48 heures avec relais aux anti-aggrégants plaquettaires (dipyridamole-Aspirine). L'appréciation de l'efficacité hémodynamique de la dilatation ou de la recanalisation a été faite par les mesures des gradients transsténotiques. Ceux-ci sont plus fiables à l'étage iliaque que fémoro-poplité du fait de la taille des artères.

Les vérification anatomo-pathologiques[4] ont permis de visualiser l'indéformabilité de la plaque d'athérome; sous l'effet de la pression, elle se rompt sur la media et l'adventice qui, par leur élasticité, se prêtent sans rupture à la dilatation. La cicatrisation intimale secondaire se fait sans rétraction fibreuse ce qui explique la persistance du "recalibrage" La cicatrice rétractile explique peut-être les récidives observées. Dans un quart des cas, après ATP, il persiste un aspect radiologique de dissection s'expliquant par ces ruptures sous-intimales. En aucun cas la réalisation d'une ATP n'a entravé secondairement un geste de chirurgie. Les complications chirurgicales sont appréciées à 3.5% par Roberts et Ring,[5] dominées dans 1% à 2% des cas par des hémorragies au point de ponction et, dans 1% des cas, par une migration embolique détériorant le lit d'aval. Dans un cas (1%) de notre série, une désobstruction par cathéter de Fogarty a été nécessaire. Schneider et collaborateurs[6] rapportent, sur 882 cas d'ATP, un taux de complications chirurgicales de 2.5% (2% de sutures artérielles et 0.5% d'emboles). Le taux d'échecs de notre série lié directement à la méthode est de 10%; il s'agit soit d'une sténose franchie non dilatée ou d'une thrombose secondaire. Le taux d'échec de l'étude collective rapportée par Zeitler et collaborateurs[7] sur 2942 cas d'ATP est aussi de 10%. Schneider et collaborateurs[6] évaluent le taux de succès initial entre 93% pour les ATP iliaques et 88.3% pour les atteintes fémoro-poplitées. Levade et collaborateurs[8] rapportant les résultats de l'étude multicentriques française sur 647 cas d'ATP, observent 6% de complications (dont 2% chirurgicales) et un taux de succès de 96% à l'étage iliaque et 92% à l'étage sous-crural. Rieger et collaborateurs,[9] sur 306 sténoses iliaques, observent 88.3% de succès immédiat.

Tardivement l'évaluation des résultats repose sur l'amélioration clinique et hémodynamique ainsi que sur d'éventuels contrôles radiologiques. La mesure des indices systoliques à la cuisse et à la cheville permet d'authentifier un bon résultat ainsi que les épreuves de marche avec étude de la récupération des valeurs de repos.[10,11] Samson et collaborateurs[12] décrivent une possible dissociation anatomoclinique: dans 9 cas sur 12 d'ATP iliaques et 3 sur 12 ATP fémoro-poplitées sans amélioration objective des chiffres hémodynamiques malgré un succès radiologique, les membres ont été sauvés. Anatomiquement, le contrôle est possible par les méthodes semi-effractives que sont les angiographies intraveineuses photographiques avec soustraction[13] ou les angiographies veineuses digitalisées.[14]

La fiabilité à long terme de l'ATP est grande. Schneider et collaborateurs[6] retrouvent un taux actuariel de perméabilité à 1 et 5 ans de 89.4% et 84.6% à l'étage iliaque et de 74% à 68% au niveau sous-crural. Sur 5000 cas recensés par Zeitler et collaborateurs,[7] le taux de perméabilité à 3 ans à l'étage iliaque est de 84% et, à 5 ans à l'étage fémoro-poplité, de 69%. Rieger et collaborateurs[9] ont retrouvé un taux de perméabilité à 6 ans de 80% sur 164 sténoses iliaques contrôlées.

Ainsi l'indication idéale de l'ATP est-elle représentée par le sténose courte, concentrique et non calcifiée de l'artère iliaque primitive ou de l'artère iliaque externe.[5,15] À l'étage fémoral c'est surtout l'artère fémorale superficielle qui est l'objet de la dilatation. Ces indications sont élargies aux artères iliaques internes, fémorales profondes et au sténoses anastomotiques.[5]

Conclusions

Le taux important de succès initial et à long terme de cette technique peu agressive et non chirurgicale lui réserve une place de choix dans le traitement de cette maladie chronique qu'est l'artériopathie des membes inférieurs. Les limites techniques de l'ATP, progressivement reculées, permettent d'élargir les indications. Loin d'être une thérapeutique concurentielle de la chirurgie, l'ATP en est un complément. Peut-être la décennie à venir élargira-t-elle les possibilités de l'angiographie thérapeutique par l'application du rayon laser sur la plaque d'athérome.

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BOOKS RECEIVED

This list is an acknowledgement of books received. It does not preclude review at a later date.

Arthoscopy: Diagnostic and Surgical Practice. S. Ward Casscells. 192 pp. Illust. Lea & Febiger, Philadelphia, 1984. $50. ISBN 0-8121-0888-4.

Atlas of Stomal Pathology. A. Franchini, B. Cola and P.J. d'E. Stevens. 112 pp. Illust. Raven Press, New York, 1983. $70 (US). ISBN 88-85937-37-2.

Blood Platelet Function and Medicinal Chemistry. Edited by Andrew Lasslo. 324 pp. Illust. Elsevier Science Publishing Co., Inc., New York, 1984. $49.50 (US), paperbound. ISBN 0-444-00790-3.

Complications in Surgery and Trauma. Edited by Lazar J. Greenfield. 945 pp. Illust. J.B. Lippincott Company, Philadelphia, 1984. $75 (US). ISBN 0-397-50521-3.

Enteral and Tube Feeding. Clinical Nutrition. Volume I. John L. Rombeau and Michael D. Caldwell. 610 pp. Illust. W.B. Saunders Company Canada Limited, Toronto, 1984. $65.35. ISBN 0-7216-7644-8.

New Approaches to the Study of Benign Prostatic Hyperplasia. Proceedings of the Ninth Brook Lodge Workshop on Problems in Reproductive Physiology, held in Augusta, Michigan, September 26–27, 1983. Edited by Frances A. Kimball, Allen E. Buhl and Donald B. Carter. 394 pp. Illust. Alan R. Liss, Inc., New York, 1984. $56 (US). ISBN 0-8451-0145-5.

Orthopaedics. Principles and Their Application. 4th ed. 2 vols. Samuel L. Turek. 1756 pp. Illust. J.B. Lippincott Company, Philadelphia, 1984. $125 (US). ISBN 0-397-50604-X.

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THOMAS H. ANDERSON, MD; MERVYN DEITEL, MD, FRCS[C], FACS

Duodenal Obstruction Secondary to Congenital Web in an Adult

Congenital duodenal web, although rare, may be more common than presently appreciated. The possibility of this condition should be considered in the differential diagnosis of duodenal obstruction in the adult. It should be treated surgically either by duodenotomy with excision of the web or by duodenojejunostomy. The results are excellent, as illustrated by the authors in their report of a 58-year-old man with this condition, who was treated by duodenojejunostomy.

Bien que rare, la présence d'un diaphragme duodénal congénital est peut-être plus fréquente qu'on ne le croit présentement. Cette possibilité doit être envisagée chaque fois que l'on procède au diagnostic différentiel d'une obstruction duodénale chez l'adulte. Cette affection est une indication de chirurgie. L'opération consiste en une duodénotomie avec incision de la membrane ou en une duodéno-jéjunostomie. Les résultats sont excellents comme l'illustre le cas décrit par les auteurs d'un homme de 58 ans qui a été traité par duodéno-jéjunostomie.

Congenital duodenal diaphragm or web is a rare anomaly, reported to occur in 1 in 9000 to 40 000 births.[1] The majority become apparent in infancy. Its occurrence in adults has been considered a rarity, but recent reports suggest that this entity may be more common than previously appreciated.[1-3] Appropriate investigations include plain films of the abdomen, upper gastrointestinal series and gastroduodenoscopy. Once the diagnosis is made, operation is indicated.

We report a case of congenital web which presented with acute duodenal obstruction in an adult and was diagnosed preoperatively. Excellent results were obtained with a duodenojejunostomy.

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Case Report

A 16-hour history of progressive abdominal distension, epigastric fullness and one episode of vomiting led to the admission of a 58-year-old man. He denied a history of peptic ulcer disease, weight loss or malaise. He admitted that he had suffered intermittently for many years from epigastric fullness and mild discomfort following the ingestion of high residue foods, particularly raw fruits and vegetables, but because this occurred infrequently he had never sought medical attention. He was a well-nourished, mildly obese, afebrile man who complained of mild discomfort and had marked upper abdominal distension. There were no signs of peritoneal irritation and bowel sounds were normal. His hemoglobin, serum electrolyte and blood urea nitrogen levels were normal. The leukocyte count was slightly elevated. Abdominal films showed a markedly distended stomach (Fig. 1). Following insertion of a nasogastric tube, 1.5 L of bile-stained fluid were aspirated.

Roentgenography after barium meal showed that the first and second portions of the duodenum were distended (Fig. 2a) and there was partial obstruction at the third portion (Fig. 2b). A septum was outlined at the point of obstruction, with the contrast medium trickling through a centrally located aperture.

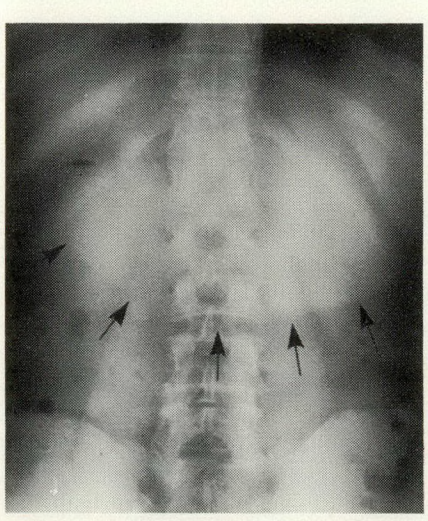

FIG. 1—Plain film shows stomach distended with fluid.

Ultrasonography revealed a normal gallbladder, biliary tree and pancreas.

Endoscopy, using the 11-mm Q-gastroscope, revealed a normal esophagus, a large stomach containing bile-stained material, a dilated pylorus and first, second and proximal third parts of the duodenum. There was no duodenal ulcer. At the proximal third part of the duodenum, approximately 7 cm beyond the ampulla of Vater, was a circumferential, soft, mucosa-lined diaphragm with a central opening. The endoscope could be passed with difficulty through the centrally located aperture, the margins of which hugged the instrument.

At laparotomy on the day of admission, a

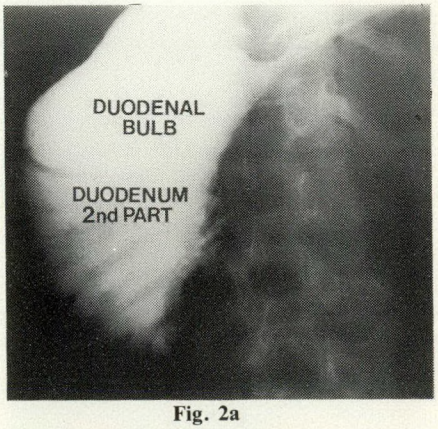

Fig. 2a

Fig. 2b

FIG. 2—(a) Markedly distended first and second portions of duodenum. (b) Almost complete obstruction of proximal third part of duodenum due to septum with tiny central opening.

normal gallbladder and pancreas were noted. The first, second and proximal part of the third portions of the duodenum were dilated and mobilized by the Kocher maneuver. There was no evidence of compression of the duodenum by the superior mesenteric artery, the obstruction being to the right of this vessel. The duodenum was marked externally by a slight ring-like constriction at the site of obstruction.

A side-to-side antecolic duodenojejunostomy was performed. The postoperative recovery was uncomplicated. At the 6-month follow-up, the patient was asymptomatic, experiencing no epigastric fullness or discomfort with high-residue foods. An upper gastrointestinal series showed that the duodenojejunostomy emptied promptly.

Discussion

Forty-three cases of congenital duodenal web presenting in adults have been reported,[1] 5 in the past 2 years.[2,3] Some patients had moderate to severe symptoms of upper gastrointestinal tract obstruction intermittently for several months to a few years. Outlet obstruction attributed directly to peptic ulcer disease was the most common preoperative diagnosis in these cases.[1-4] In the three patients described by Cooperman and associates[1] and in two of three patients reported by Killebrew and Kukora,[3] conservative therapy resulted in marked prolongation of obstructive symptoms with resulting malnutrition.

The embryologic defect producing the duodenal web is probably best explained by Tandler's theory, proposed in 1900.[5] Tandler examined the developing gut in embryos and found that during its development the intestinal lumen is filled with proliferating epithelium. A process of vacuolization results in a lumen. If vacuolization is incomplete, a duodenal web may result. Atresia of the intestinal lumen also occurs as a result of incomplete vacuolization. A complete web becomes manifest in the neonate. When apertures are present, they may be single or multiple. One patient, reported by Bilton and Yap,[6] had a single 2-mm aperture that did not become clinically apparent until age 61.

It is not clearly understood why patients with small apertures may live for many years asymptomatically, in a normal nutritional state, and then the condition may progress to obstruction. In at least six reported cases the obstruction occurred concomitantly with pyloroduodenal ulceration. Subsequent medical ulcer therapy resulted in only temporary relief of the obstruction.[1-3] Mucosal edema associated with the ulcer with resultant narrowing of the aperture distally may have caused the condition to progress to obstruction in these patients. Intermittent partial duodenal obstruction by debris following high-residue meals and mucosal edema are likely an important cause. We believe this explains the development of obstruction in our patient.

The diagnosis of duodenal web in an adult requires an awareness of the entity, in order to distinguish it from the other uncommon causes of high small-bowel obstruction, such as superior mesenteric artery syndrome[7,8] and annular pancreas.[9] Plain abdominal roentgenograms may show dilated stomach and proximal duodenum. The upper gastrointestinal series will demonstrate the dilated stomach and duodenum proximal to the web and may show a windsock-shaped obstruction (Fig. 2b). Gastroscopy was used in seven other cases,[1-3,10] but was carried through the duodenum far enough to give the diagnosis preoperatively in only three; the diagnosis was confirmed by gastroduodenoscopy in our patient.

Intraoperatively, the presence of a slight circumferential indentation of the duodenum externally indicated the site of the web. Histologically, the web consists of a lining of thickened mucosa, including muscularis mucosae, on both sides of a normal submucosa.[5] Of these duodenal webs, 75% are within 2 cm of the ampulla of Vater;[1,5] approximately 60% are located proximal to the ampulla.[3]

Initial therapy consists of gastric decompression with a nasogastric tube and replacement of fluid and electrolytes. The surgical procedures that have been performed include duodenotomy with excision of the web and duodenoplasty,[1,3,6,10] duodenojejunostomy,[8] gastrojejunostomy[3,6] and duodenoduodenostomy.[2,11] Most patients have been treated by duodenotomy with excision of the web and suturing the mucosal edges together, with either a transverse or longitudinal closure of the duodenotomy or Finney pyloroplasty.[1-3,6,10] This gives excellent results. Gastrojejunostomy may be inadequate, as it fails to relieve the duodenal obstruction and symptoms often persist postoperatively.[4] Furthermore, bile gastritis may recur subsequently. We preferred duodenojejunostomy in our patient, because the web was approximately 7 cm beyond the ampulla and quite close to the superior mesenteric artery. Technically, this was easily performed.

Our patient differed in that he had a brief history of obstructive symptoms. The normal electrolyte levels, fluid balance and nutritional status of the patient support this. However, the fact that he had a markedly distended stomach and duodenum and yet had vomited only once and was not in severe distress indicated that there was a degree of chronic obstruction.

The congenital duodenal web, although rare, is likely more common than has been appreciated, with three papers being published recently, reporting on eight adult patients.[1-3] This entity should be considered in the differential diagnosis of subacute or acute duodenal obstruction in the adult. Once the diagnosis is made, surgical correction either by duodenotomy with excision of the web or a duodenojejunostomy provides excellent results.

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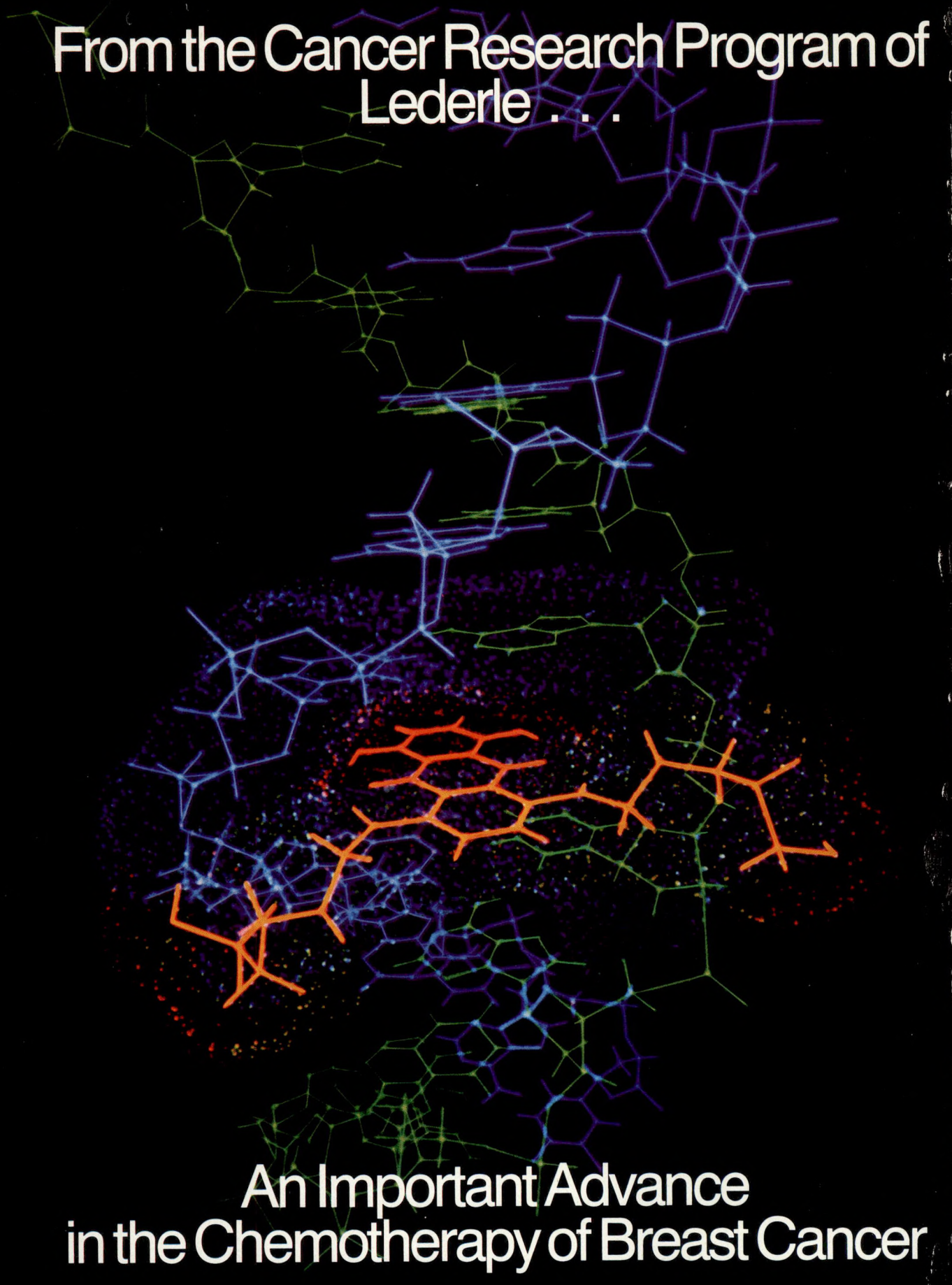
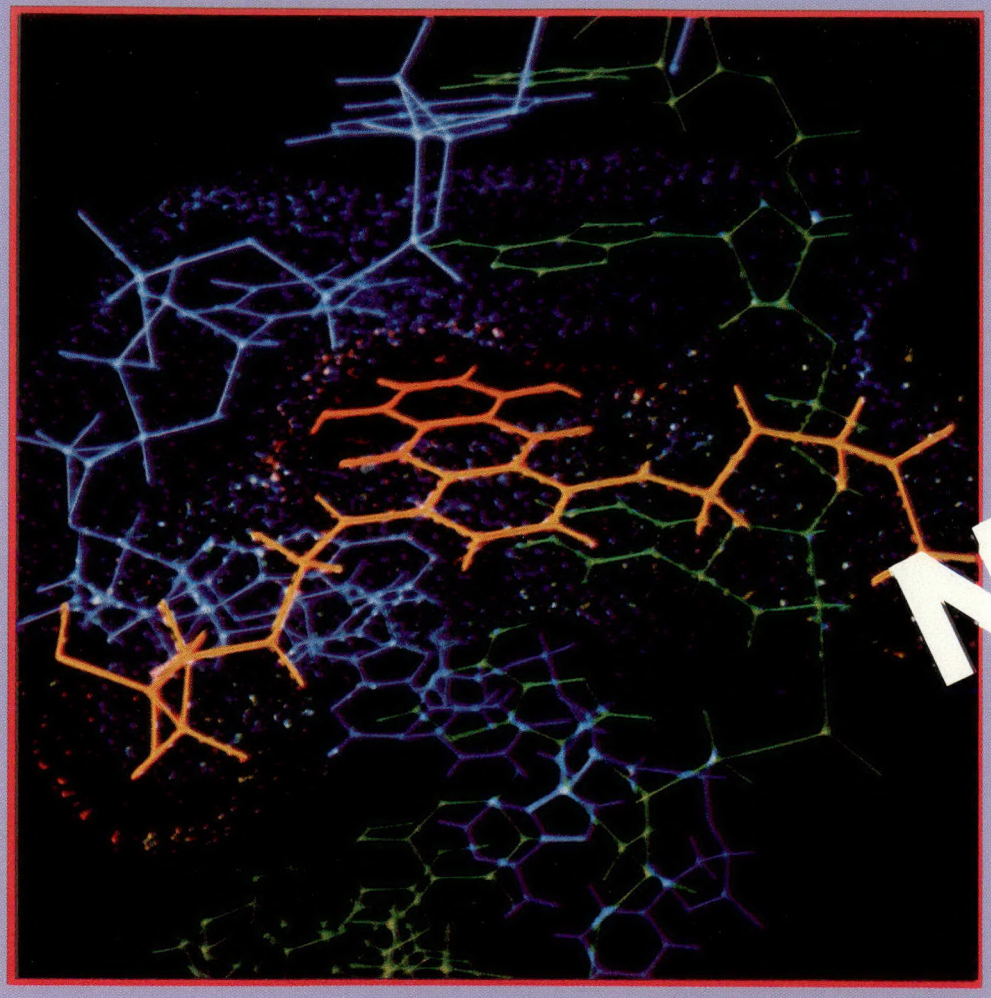
From the Cancer Research Program of Lederle . . .



An Important Advance in the Chemotherapy of Breast Cancer

One of the Most Active Single Agents in Advanced Breast Cancer...



NEW

Activity comparable to doxorubicin

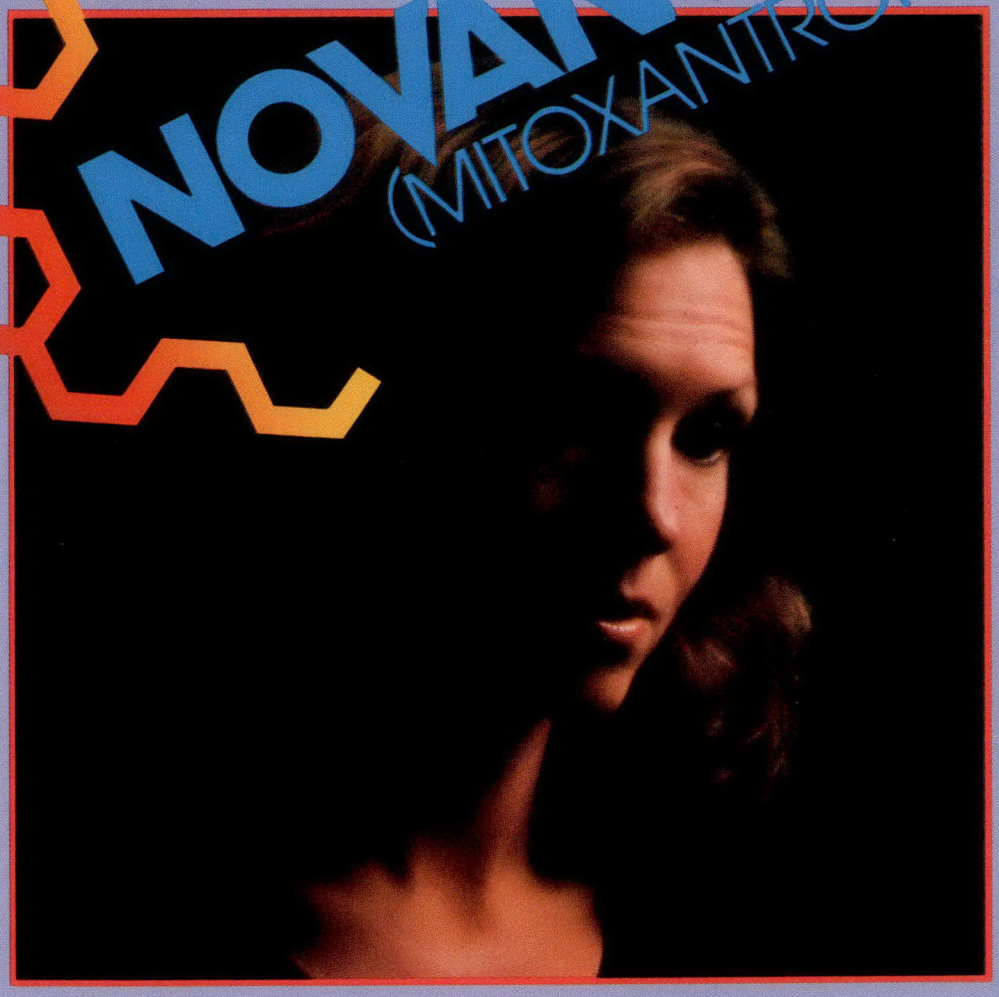
Effective as first and second line therapy

Responses at all major sites of metastases

Long duration of response

With Proven Quality of Life Benefits

NOVANTRONE* (MITOXANTRONE)



Less than 6% severe alopecia

Little or no severe nausea and vomiting

No tissue necrosis on extravasation reported

Low potential for cardiotoxicity

NOVANTRONE*

mitoxantrone hydrochloride
intravenous injection

ANTINEOPLASTIC AGENT

CAUTION

NOVANTRONE* IS A POTENT DRUG AND SHOULD BE USED ONLY BY PHYSICIANS EXPERIENCED WITH CANCER CHEMOTHERAPEUTIC DRUGS (SEE WARNINGS AND PRECAUTIONS). BLOOD COUNTS SHOULD BE TAKEN AT FREQUENT INTERVALS PRIOR, DURING AND POST THERAPY. CARDIAC MONITORING IS ADVISED IN THOSE PATIENTS WHO HAVE RECEIVED PRIOR ANTHRACYCLINES, PRIOR MEDIASTINAL RADIOTHERAPY OR WITH PRE-EXISTING CARDIAC DISEASE.

PHARMACOLOGICAL ACTION

Although its mechanism of action has not been determined, mitoxantrone is a DNA-reactive agent. It induces nuclear aberrations with chromosome scattering in cell cultures (human colon carcinoma line) and is a potent inhibitor of RNA and DNA synthesis. Compared on an equimolar basis, mitoxantrone is seven times more potent than doxorubicin in inhibiting the uptake of ^{3}H-uridine and four times more potent in inhibiting the uptake of ^{3}H-thymidine by mouse lymphoma L5178Y cells in vitro.

INDICATIONS

NOVANTRONE* is indicated for chemotherapy in patients with carcinoma of the breast, including locally advanced and metastatic disease.

CONTRAINDICATIONS

NOVANTRONE* is contraindicated in patients who have demonstrated prior hyper- sensitivity to anthracyclines.

WARNINGS

Since NOVANTRONE* produces myelosuppression (see ADVERSE EFFECTS), it should be used with caution in patients in poor general condition or with pre-existing myelosuppression.

Cases of functional cardiac changes, including congestive heart failure and decreases in left ventricular ejection fraction have been reported. These cardiac events have occurred almost exclusively in patients who have had prior treatment with anthracyclines, prior mediastinal radiotherapy or with pre-existing heart disease. Cardiac monitoring is advisable in such patients. It is suggested that cardiac monitoring also be performed in other patients during therapy exceeding 12 courses of NOVANTRONE*, as experience during prolonged treatment is limited.

NOVANTRONE* may impart a blue-green colouration to the urine for 24 hours after administration, and patients should be advised to expect this during active therapy. Safe use of NOVANTRONE* in pregnancy has not been established. No information is available concerning the presence of NOVANTRONE* in the milk of nursing mothers.

PRECAUTIONS

Full blood counts should be undertaken serially during a course of treatment. Dosage adjustments may be necessary based on these counts (see DOSAGE section).

It is recommended that NOVANTRONE* not be mixed in the same infusion with other drugs.

ADVERSE EFFECTS

NOVANTRONE* is clinically well tolerated, demonstrating a low overall incidence of adverse events, particularly those of a severe, irreversible or life-threatening nature.

Some degree of leukopenia is to be expected following recommended doses of NOVANTRONE*. However, suppression of WBC counts below 1000/mm^3 is infrequent. With dosing every 21 days, leukopenia is usually transient, reaching its nadir at about 10 days after dosing, with recovery usually occurring by the 21st day. Thrombocytopenia can occur, and anaemia occurs less frequently. Myelosuppression may be more severe and prolonged in patients having had extensive prior chemotherapy or radiotherapy or in debilitated patients.

The most commonly encountered side effects are nausea and vomiting, although in the majority of cases these are mild (WHO Grade 1) and transient. Alopecia may occur, but is most frequently of minimal severity and reversible on cessation of therapy.

Other side effects which have occasionally been reported include anorexia, diarrhoea, dyspnoea, fatigue and weakness, fever, gastrointestinal bleeding, stomatitis/ mucositis, and non-specific neurological side effects.

Changes in laboratory test values have been observed infrequently, e.g., increased liver enzyme levels, elevated serum creatinine and blood urea nitrogen levels.

Cardiovascular effects, which have only occasionally been of clinical significance, include decreased left ventricular ejection fraction (determined by ECHO or MUGA scan), EKG changes and acute arrhythmia. Congestive heart failure has been reported. Such cases generally responded well to treatment with digitalis and/or diuretics.

CLINICAL RESULTS

Introduction

Clinical trials experience has established the dosage range, efficacy and safety profile of NOVANTRONE*.

A single dose can be given intermittently every three or four weeks. The recommended initial treatment dose in good risk patients is 14 mg/m^2.

Efficacy

Efficacy data are available on 349 patients with locally advanced or metastatic breast carcinoma. Results are dependent on many predisposing factors including prior chemotherapy and/or radiotherapy, the health of the patients, sites of metastases, and dose of the agent employed. In a European multi-centre first- line single-agent trial using an initial dose of 14 mg/m^2, the overall response rate was 39%, which compared favourably to doxorubicin therapy at a dose of 60-75 mg/m^2 when given to patients with similar stage disease. In an ongoing study of a direct comparison with doxorubicin, given as second-line therapy to breast cancer patients who failed a standard first-line combination, response rates are 27% for NOVANTRONE* and 23% for doxorubicin. The mean duration of response observed after NOVANTRONE* was greater than those reported after doxorubicin. Responses have been seen in all major sites of metastases including lymph nodes, lung, bone, skin and viscera, in patients both with and without prior hormonal therapy. Available data suggest that NOVANTRONE* is comparable in efficacy with doxorubicin in the treatment of advanced breast cancer. Myelosuppression with 21-day treatment intervals is comparable with that observed with doxorubicin. Multiple courses of single-agent NOVANTRONE* therapy, in some cases for longer than twelve cycles, have been administered with excellent tolerance and a good response. NOVANTRONE* showed incomplete cross-resistance with doxorubicin since responses have been observed in patients in whom doxorubicin had failed or who relapsed after response to that drug. A continuing large-scale clinical trials program with combination therapy also demonstrated early positive results for efficacy and safety. In seven studies, over 100 cycles of combination therapy have been given to 77 patients.

Safety

Data on the overall safety profile of NOVANTRONE* (based on 989 patients) demonstrated advantages of NOVANTRONE* compared to the anthracyclines with respect to both the quality of life and the long-term safety of patients. The majority of side effects with NOVANTRONE* are mild in nature. Removal of patients from NOVANTRONE* treatment for reasons of toxicity has been rare in clinical studies. A number of patients have reported no side effects at all. In addition, the relatively low risk of serious side effects has permitted treatment of patients on an out-patient basis. The most common acute effects were nausea and/or vomiting (only 3.5% severe or very severe with NOVANTRONE*, compared to 10-15% reported with doxorubicin), stomatitis/mucositis (only 0.3% severe or very severe with NOVANTRONE*) and alopecia (only 0.9% severe or very severe, and 15% overall with NOVANTRONE* compared with 85% severe or very severe and 100% overall reported with doxorubicin). Serious local reactions have not been reported following extravasation of NOVANTRONE* at the infusion site.

With respect to myelosuppression, initial NOVANTRONE* doses of 14 mg/m^2 every three weeks are well-tolerated in good-risk patients. Severe degrees of myelosuppression have been rare. The median white cell nadir in a European second-line study was 2.5x10^3; in a European first-line study only 4.8% (2/42) of patients experienced a nadir of less than 1,000. The nadir usually occurs around day 10 or 11 and returns to normal baseline value by day 21, in time for the next course of treatment. After multiple courses of NOVANTRONE*, white blood cell and platelet nadirs show no further decrease beyond those observed in the first few cycles, indicating no cumulative or permanent effects of NOVANTRONE* on marrow reserves.

Cardiotoxicity

Adverse cardiac experiences have been infrequent. In contrast, doxorubicin has been reported to produce chronic cardiomyopathy and irreversible congestive heart failure in up to 11% of patients given nine or more courses of that drug at the usual dose schedule (60 mg/m^2 every three weeks). Whether or not related to NOVANTRONE*, only 119 cardiac-related episodes have been reported from a total data-base of more than 3,200 treated patients, including only 29 (0.9%) reports of clinical congestive heart failure, of which only one had no other known predisposing factors. The risk of cardiotoxicity is increased with prior antineoplastic drug or radiation therapy. In patients without predisposing factors, development of congestive heart failure with NOVANTRONE* therapy is rare.

Clinical experience suggests there is no need to lower the dose for patients with existing renal or hepatic disease.

In summary, NOVANTRONE* is well tolerated and provides a better quality of life for patients with breast cancer, compared with doxorubicin and yet shows comparable efficacy.

NOVANTRONE* has been used alone or in combination in patients with or without prior chemotherapy, as well as in those who have received prior adjuvant therapy. It is less cardiotoxic than anthracyclines such as doxorubicin and thus represents a clear therapeutic advance over currently available compounds.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

There is no known specific antidote for NOVANTRONE. As would be expected from the pharmacological actions of the drug, haematopoietic, gastrointestinal, hepatic and renal toxicity may be seen, depending on the dosage given and the physical condition of the patient. The management of overdosage is symptomatic and supportive and patients should be monitored closely. (See also the sections "WARNINGS", "PRECAUTIONS" and "ADVERSE REACTIONS")

DOSAGE

The recommended initial dosage for use as a single agent is 14 mg/m^2 of body surface area, given as a single intravenous dose, which may be repeated at 21-day intervals. A lower initial dose (12 mg/m^2 or less) is recommended in patients with inadequate marrow reserves due to prior therapy or poor general condition.

Dosage modification and timing of subsequent dosing should be determined by clinical judgement depending on the degree and duration of myelosuppression. If 21-day white blood cell and platelet counts have returned to adequate levels, prior doses can usually be repeated. The following Table indicates a guide to dosing based on myelosuppression.

WBC AND PLATELET NADIR	TIME TO RECOVERY	SUBSEQUENT DOSING
IF WBC NADIR >1 500 AND PLATELET NADIR >50 000	RECOVERY ≤21 DAYS	REPEAT PRIOR DOSE OR INCREASE BY 2mg/m^2 IF MYELOSUPPRESSION NOT CONSIDERED ADEQUATE.
IF WBC NADIR >1 500 AND PLATELET NADIR >50 000	RECOVERY >21 DAYS	WITHHOLD UNTIL RECOVERY THEN REPEAT PRIOR DOSE.
IF WBC NADIR <1 500 OR PLATELET NADIR <50 000	ANY DURATION	DECREASE BY 2mg/m^2 FROM PRIOR DOSE AFTER RECOVERY.
IF WBC NADIR <1 000 OR PLATELET NADIR <25 000	ANY DURATION	DECREASE BY 4 mg/m^2 FROM PRIOR DOSE AFTER RECOVERY.

While no unforeseen problems have been encountered when NOVANTRONE* is used in combination with other antineoplastic therapy, data are limited; therefore, NOVANTRONE* in combination therapy should be used with caution until wider experience is obtained.

As a guide, when used in combination chemotherapy with another myelosuppressive agent, the initial dose of NOVANTRONE* should be reduced by 2-4 mg/m^2 below the doses recommended above for single agent usage; subsequent dosing, as outlined above, depends on the degree and duration of myelosuppression.

ADMINISTRATION OF SOLUTION

NOVANTRONE* solution should be diluted to at least 50 mL with either Sodium Chloride for Injection (U.S.P.) or 5% Dextrose for Injection (U.S.P.). This solution should be introduced slowly into the tubing of a freely-running intravenous infusion of Sodium Chloride for Injection (U.S.P.) or 5% Dextrose for Injection (U.S.P.) administered over not less than three to five minutes intravenously. If extravasation occurs, the administration should be stopped immediately and restarted in another vein. However, serious local reactions have not been reported following extravasation.

NOVANTRONE* should be administered by individuals experienced in the use of antineoplastic therapy.

Caution in the handling and preparation of NOVANTRONE* solutions must be exercised and the use of protective eyeglasses, gloves and other protective clothing is recommended. (See "SAFE HANDLING BY HOSPITAL PERSONNEL" section).

STORAGE DIRECTIONS

NOVANTRONE* should be stored at room temperature — DO NOT FREEZE. With recommended storage, NOVANTRONE* remains stable for two (2) years.

Following preparation of the infusion, the diluted solution should be stored at room temperature and used within 24 hours. Any original solution which remains in the vial should be discarded. *NOTE:* LIKE THE ORIGINAL SOLUTIONS, THE DILUTIONS SHOULD ALSO NOT BE FROZEN.

DRUG COMPATIBILITY

Until specific compatibility data are available, it is recommended that NOVANTRONE* not be mixed in the same infusion with other drugs.

GUIDELINES FOR SAFE USE BY HOSPITAL PERSONNEL

Handling:

1. Preparation of antineoplastic solutions should be done in a vertical laminar flow hood (Biological Safety Cabinet — Class II).
2. Personnel preparing NOVANTRONE* solutions should wear PVC gloves, safety glasses and protective clothing such as disposable gowns and masks.
3. Personnel regularly involved in the preparation and handling of antineoplastics should have bi-annual blood examinations.

Disposal:

1. Avoid contact with skin and inhalation of airborne particles by use of PVC gloves and disposable gowns and masks.
2. All needles, syringes, vials, ampoules and other materials which have come in contact with NOVANTRONE* should be segregated in plastic bags, sealed and marked as hazardous waste. Incinerate at 1000°C or higher. Sealed containers may explode if a tight seal exists.
3. If incineration is not available, mitoxantrone hydrochloride may be detoxified by adding 5.5 parts by weight of calcium hypochlorite to each 1 part by weight of mitoxantrone hydrochloride in 13 parts by weight of water.† The calcium hypochlorite should be added GRADUALLY and the procedure carried out with adequate ventilation since chlorine gas is liberated.

Vials:

Prepare an adequate quantity of calcium hypochlorite solution (eg: Add 43.5 g calcium hypochlorite to 100 mL of water†). Withdraw any NOVANTRONE* remaining in the vial with the aid of a hypodermic syringe. Add to the prepared calcium hypochlorite solution slowly, preferably in chemical fume hood or biological safety cabinet — Class II. Add an appropriate quantity of the calcium hypochlorite solution to the vial to detoxify any remaining drug. Withdraw the solution and discard in the sewer system with running water. Dispose of the detoxified vials in a safe manner.

Needles, syringes, disposable and non-disposable equipment:

Rinse equipment with an appropriate quantity of calcium hypochlorite solution (43.5 g per 100 mL of water†). Discard the solution in the sewer system with running water and discard disposable equipment in a safe manner. Thoroughly wash non-disposable equipment in soap and water.

Spillage/Contamination:

Wear gloves, mask, protective clothing. Place spilled material in an appropriate container (i.e. cardboard for broken glass) and then in a polyethylene bag; absorb remains with gauze pads or towels; wash area with water and absorb with gauze or towels again and place in bag; seal, double bag and mark as a hazardous waste. Dispose of waste by incineration or by other methods approved for hazardous materials. Personnel involved in cleanup should wash with soap and water.

† Appropriate safety equipment such as goggles and gloves should be worn while working with calcium hypochlorite solution since it is corrosive.

AVAILABILITY

NOVANTRONE* mitoxantrone hydrochloride for injection is supplied as a sterile aqueous solution at a concentration equivalent to 2 mg mitoxantrone free base per mL, and is available in the following vial sizes:

10mL/vial (20mg) Product Code 9393-34
12.5mL/vials (25mg) Product Code 9393-72

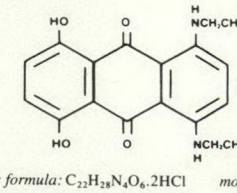
Identification:

Glass vials containing 10 and 12.5mL of a clear, dark blue solution.

CHEMISTRY

Composition

NOVANTRONE* mitoxantrone hydrochloride, a synthetic anthracenedione, is a potent antineoplastic agent. Its molecular formula is $C_{22}H_{28}N_4O_6$.2HCl and its molecular weight is 517.4. It is a hygroscopic dark blue solid supplied as a sterile, aqueous solution containing mitoxantrone hydrochloride equivalent to 2 mg/mL mitoxantrone free base, with sodium chloride, sodium acetate, and acetic acid as inactive ingredients. The product does not contain antibacterial preservatives. Its structural formula appears below.



molecular formula: $C_{22}H_{28}N_4O_6$.2HCl *molecular weight:* 517.4.

Chemical Name

1, 4-Dihydroxy-5,8-bis[[2-[(2-hydroxyethyl)amino]-ethyl] amino] -9,10-anthracenedione dihydrochloride

*Trade mark of American Cyanamid Company

Lederle

Cyanamid Canada Inc.
Toronto

PAAB
CCPP

Product monograph available on request.

R.A. HANCOCK, MD; T.E. HODGINS, MD, FRCS[C]

The Prone Position for Transurethral Resection of Anterior Bladder-Wall Tumours

Transurethral resection of tumours of the anterior bladder wall may be technically difficult. The resectoscope must be held with an awkward upside-down grip and the surgeon assume an uncomfortable position, particularly as the bladder fills and causes the tumour to drift away from the surgeon. There is a risk of intraperitoneal perforation as the surgeon cuts more deeply to resect the tumour. When the patient is in the prone position the tumour is more accessible. This allows it to be resected more easily, more thoroughly and more comfortably. The technique may be used in men as well as in women.

La résection transurétrale des tumeurs de la paroi antérieure de la vessie peut présenter des difficultés techniques. La prise du resectoscope est difficile et le chirurgien conserve une position inconfortable, particulièrement quand la vessie se remplit, poussant la tumeur hors de la portée du chirurgien. Alors que le chirurgien doit sonder plus profondément pour réséquer la tumeur, il y a risque de perforation intrapéritonéale. La tumeur est plus facilement accessible quand le patient est couché sur le ventre. Ceci permet une résection plus facile, plus complète et plus confortable. La technique s'applique aussi bien chez l'homme que chez la femme.

Transurethral resection is an excellent method of treating patients with the common, superficial stage 0, A or B1 carcinoma of the bladder and as palliation for some patients with stage C or D tumours (Jewett classification[1] with the Marshall modification[2]). The procedure is technically simple, the morbidity and mortality are low and bladder function is preserved. These benefits are related, to some extent, to the experience of the surgeon and to the fact that most bladder cancers are found near the ureteral orifices. Melicow[3] noted that, in 70% of patients, the carcinomas are found on the posterior and lateral wall near the ureteral orifices, 20% are found on the trigone and in only 10% of patients do the tumours occur on the dome of the bladder. Cox and associates[4] reported that 44% of carcinomas are found on the lateral wall, 26% at the base of the bladder and only 13% are located on the dome. In 17% of the patients the lesions were multiple.[4] Greene and associates[5] noted that more than 80% of carcinomas of the bladder are related anatomically to the ureteral orifice and only 9% are found on the anterior bladder wall (Table I).

The tumours, which are found anteriorly near the 12 o'clock position, are often silent and thus more advanced when the diagnosis is made. A few are high-grade adenocarcinomas reflecting a urachal origin. Anterior bladder-wall tumours are technically more difficult to handle with a resectoscope because the instrument must be held in an awkward upside-down grip. Moreover, the surgeon often needs to assume an uncomfortable position and, as the bladder fills, the tumour drifts away from the resectionist, forcing him to "reach" to continue to resect the tumour. In some cases, an assistant must apply suprapubic pressure. There is the added risk of intraperitoneal perforation of the bladder as the surgeon resects more deeply to remove all the carcinoma.

Some years ago, the senior author (R.A.H.), faced with the problem of a carcinoma in the anterior wall of the bladder in a woman, suggested that the tumour could be resected more thoroughly, more easily and more comfortably with the patient in the prone position.[6] In this position, the anterior wall of the bladder has the same relation to the resectionist as the trigone and posterior wall of the bladder have in the lithotomy position.

Table I—Location of Bladder Tumours[3]

Location	No.	%
Posterolateral to ureteral orifices	55	46
Lateral wall	26	22
Base	14	12
Trigone	3	2
Dome, anterior wall	11	9
Vesical neck	7	5
Posterior wall	5	4

We would like to draw attention to this suggestion and extend its applicability to men. In men, an external perineal urethrotomy is needed with the urethrotomy as proximal in the perineal urethra as possible, so there will be a "straight shot" through the prostatic urethra into the bladder.

Surgical Technique

The procedure may be done with the patient under general or spinal anesthesia.

The patient is in the usual lithotomy position when the diagnostic cystoscopic examination is made. The resectoscope sheath is passed through the urethra in women or the urethrotomy in men. The foot section of the operating table, lowered for the cystoscopic examination, is elevated into place and the patient's legs are lowered onto the foot section. The patient, with the resectoscope sheath in situ, is turned to the prone position, with the legs straight and together so that the resectoscope sheath is supported by the medial aspect of the thighs. The resectoscope sheath may be wrapped with a sterile towel and held by the surgeon. The patient is placed so that the abdomen lies on the middle section of the table, pushing the anterior bladder wall into a flattened and more accessible position for the resectionist. An arm board is secured to each side of the middle section of the surgical table in a slightly abducted position and the legs are strapped to the arm boards. The foot section of the table is lowered completely to provide room for the resectionist. The operative site is prepared once more.

When the anterior lobe of the prostate is enlarged, a certain effort must be made to elevate the ocular end of the resectoscope so that the loop may bite deeply into the tumour. Sometimes the anterior

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lobe of the prostate must be resected. When the procedure is completed, a no. 24 French Foley catheter is left in the bladder for 6 days. In men, the Foley catheter is introduced with the patient supine and traverses the entire urethra. The perineal incision is packed with iodoform gauze to control bleeding. Several catgut sutures in the skin hold the packing in place for 4 days.

Comment

The benefits of the prone position are several. The resectionist can use the resectoscope in a comfortable and familiar fashion. The tumour does not drift away from the resectionist as the bladder fills. These advantages allow a more careful and thorough resection.

There is concern about implantation of malignant cells in the tract of the external perineal urethrostomy. We have not seen this. Experience in similar situations, transperineal or transrectal needle biopsy of the carcinomatous prostate,[7] transurethral resection of carcinoma of the prostate by way of an external perineal urethrostomy[8] and transurethral resection of the prostate and bladder carcinoma at the same sitting,[9] suggests that seeding is rare. We believe that the ability to resect tumours of the anterior bladder wall easily and thoroughly when the patient is in the prone position far outweighs the risk of planting carcinoma in the surgical tract.

We have found use of the prone position an excellent modification when resecting the sometimes difficult or almost impossible-to-reach tumours of the anterior bladder wall.

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Human Atrial Trabeculae: an Experimental Preparation for Studying Myocardial Response to Perioperative Manipulations

Trabeculae taken from discarded human right atrial specimens during cardiac surgery provide a useful preparation for studies in myocardial physiology and pharmacology. Three extrinsic measurements that have a marked effect on contraction of this preparation are temperature, stimulation frequency and calcium ion (Ca^{2+}) concentration. There is a large decline in developed force below 30°C. The optimal stimulation frequency (temperature 34°C, Ca^{2+} concentration 2.5 mM) is 1 Hz. The Ca^{2+} level required to give half maximal force development is 2.0 mM. In a series of 46 atrial trabeculae (approximately 1 mm in diameter) from 33 patients, the authors found a mean contraction tension of 1.37 ± 0.09 g/mm² (± standard error) (temperature 34°C, stimulation frequency 1 Hz, pH 7.4, Ca^{2+} concentration 2.5 mM) at maximum force. The preparation appears to have great potential for the study of perioperative manipulation on myocardial function.

Les colonnes charnues prélevées sur les pièces d'oreillette humaine retirées au cours d'une chirurgie cardiaque offrent une préparation utile pour l'étude de la physiologie et de la pharmacologie du myocarde. Trois facteurs extrinsèques qui exercent un effet notable sur la contraction de cette préparation sont la température, la fréquence de contraction et la concentration des ions calciques (Ca^{2+}). On constate une baisse importante de la tension développée sous les 30°C. La fréquence optimale de stimulation (à 34°C et à une concentration de Ca^{2+} de 2.5 mM) est de 1 Hz. Le taux de Ca^{2+} nécessaire pour assurer la moitié de la force maximale de développement est de 2.0 mM. Dans une série de 46 colonnes charnues auriculaires (d'environ 1 mm de diamètre) provenant de 33 patients, les auteurs ont trouvé une tension de contraction de 1.37 ± 0.09 g/mm² (± l'erreur type) (à 34°C, fréquence de stimulation de 1 Hz, pH de 7.4, concentration de Ca^{2+} de 2.5 mM) à force maximum. Cette préparation semble offrir de grandes possibilités pour l'étude des manipulations periopératoires sur la fonction myocardique.

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Myocardial tissue from human atria is available on a regular basis in centres where open-heart surgery is performed. This tissue is potentially valuable for studying the mechanics of human myocardium. Further, it may be used to study the effects of myocardial interventions, including cardioactive drugs, without the need to extrapolate from animal models.

The effects of drugs on human atrial tissue have been reported in the literature,[1-9] but it is not easy to compare and evaluate the results. The difficulty arises because preparations lack uniformity and the extrinsic variables such as stimulation rate and temperature differ. Variations in the state of the preparations are perhaps an even more serious problem and this clearly should be evaluated in each preparation. To do this, some standardized measure of contractile performance is required to provide a criterion for comparing and screening preparations. A reasonable number of measurements under standardized conditions are needed so that acceptable limits may be defined.

We have developed a standardized procedure for obtaining reasonably uniform preparations from human atria. In this report we examine 46 such preparations. Maximum contraction tension is evaluated under a defined set of conditions and

the effects of the main extrinsic determinants of myocardial contraction (temperature, stimulation frequency, pH and calcium ion concentration) are surveyed.

Methods

Samples of right atrial appendages were obtained from consenting patients at the time of cardiac surgery. Immediately after removal from the patient, the samples were immersed in oxygenated blood at 4°C and transported to the laboratory.

The endocardial surface was examined for trabeculae approximately 1 mm in diameter and 5 mm to 10 mm long. Two suitable trabeculae could usually be found in most atrial samples. The trabeculae were removed and held vertically. The lower end was held by a fixed plexiglass clip. The upper end was attached to a force transducer (model UC 2; Gould Inc., Oxnard, Calif.) through a second clip. The position of the force transducer was measured by a Mercer micrometer gauge (model 252; St. Albans, England), with the zero reference length taken from the point at which the muscle clips touched.

The preparation was then immersed in a buffered Tyrode's solution (mM: NaCl 117, KCl 3.4, $MgSO_4$ 3.1, KH_2PO_4 1.2, $NaHCO_3$ 28, glucose 11 and $CaCl_2$ 2.5) in a 120 mL water-jacketed bath at 34°C. The bath was continuously aerated with a mixture of 95% oxygen and 5% carbon dioxide (pH 7.4).

Table I—Data from Human Right Atrial Trabeculae (n = 46)

Variable	Value
Weight, mg	6.42 ± 0.35
Length at L_{max}, mm	7.18 ± 0.24
Cross-sectional area, mm^2	0.87 ± 0.04
Force, g	
Resting	0.43 ± 0.06
Developed	1.25 ± 0.08
Tension, g/mm^2	
Resting	0.47 ± 0.06
Developed	1.37 ± 0.09

Values presented as mean ± standard error. All measured at 34°C, 1 Hz, Ca^{2+} 2.5 mM and pH 7.4.

Field stimulation was used to excite the preparation through platinum plate electrodes on either side of the muscle. Stimulus pulses (5 ms) were generated by a Grass S88 stimulator through a Grass SIU-5 stimulus isolation unit (Grass Instrument Co., Quincy, Mass.). Stimulus voltage was adjusted to a level 50% above the maximum response. Contractions were monitored on a Grass model 7 direct writing recorder from the force transducer.

After mounting, the trabeculae were allowed to equilibrate at 34°C for 20 minutes at a stimulus frequency of 0.1 Hz with a light (0.2 g) preload. Stimulus frequency was then increased to 1 Hz and length was increased until maximum force (L_{max}) was developed. Muscles were allowed to stabilize for a further 20 minutes and basal resting and active forces were measured.

This second equilibration period was used to screen out unacceptable preparations — those with contraction anomalies such as multiple peak contractions, those with spontaneous electrical activity and those with low contractile force. An arbitrary cut-off value of 0.7 g was adopted on the basis of preliminary experiments.

About half of the preparations were rejected, mainly because of spontaneous activity; 46 trabeculae remained. These preparations were taken from 33 patients (26 men, 7 women), between 20 and 68 years of age. The operative diagnoses were coronary artery disease in 27, valvular disease in 4 and congenital heart disease in 2 patients.

The effect of one variable was studied in each of four groups of preparations. In group 1 (n = 14), five different stimulation frequencies were used (0.5, 1.0, 1.5, 2.0 and 2.5 Hz). In group 2 (n = 8), force was monitored at three pH levels (6.7, 7.4 and 7.9). The pH of the Tyrode's solution was adjusted to these values by titration with 0.1 M sodium hydroxide or 0.1 M hydrochloric acid. Group 3 (n = 12) was used to study the effect of different temperatures (20°, 25°, 30°, 35° and 40°C). In group 4 (n = 12), different Ca^{2+} concentrations were used (1.5, 2.0, 2.5, 3.0, 3.5 and 4.0 mM). In all of the above interventions, changes were made in random order and after each change a stabilization period of 5 to 15 minutes was allowed before the response was measured. Preliminary experiments showed that the effects of changes in temperature, pH and frequency were reversible but that some residual effects remained after changes in Ca^{2+} concentration. To overcome this problem, the preparation was returned to a Ca^{2+} level of 2.5 mM after each change, and force with each concentration was expressed as a percentage of that in 2.5 mM Ca^{2+} immediately before each random change.

For comparative purposes the tension (g/mm^2) was calculated by dividing the measured force (g) by the cross-sectional area (mm^2). At the end of each experiment, the trabecula between the two clips was removed, blotted dry, and weighed on a Roller-Smith torsion balance (Bethlehem, Penn.). The cross-sectional area (mm^2) was then calculated by first converting the weight (mg) of the preparation into volume (mm^3) with a density of 1.065 and then dividing the volume by the length (mm) of the muscle at L_{max}, assuming the trabecula to be cylindrical.

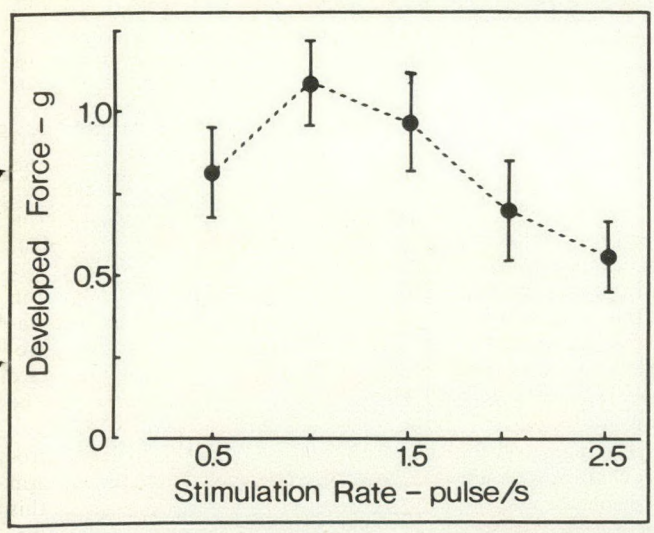

FIG. 1—Frequency–force relation; mean contractile force (circles) and standard error (vertical lines) for 14 trabeculae; pH 7.4, 34°C, Ca^{2+} concentration 2.5 mM.

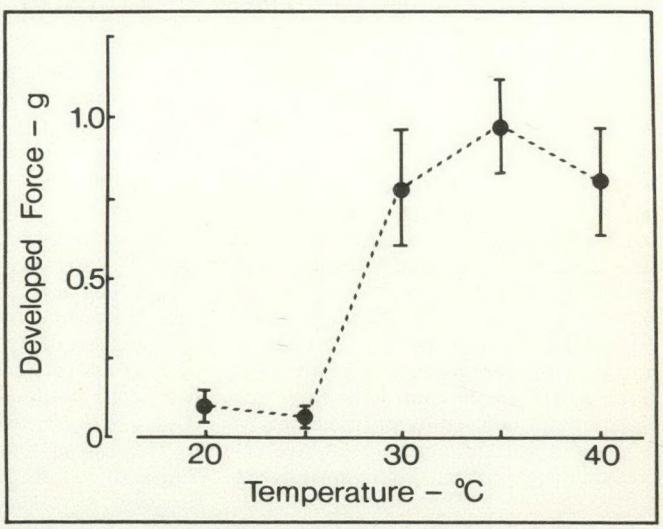

FIG. 2—Temperature–force relation; mean contractile force (circles) and standard error (vertical lines) for 12 trabeculae; pH 7.4, frequency 1 Hz, Ca^{2+} concentration 2.5 mM.

Results

During the first equilibrium period, while the muscle was stimulated at 0.1 Hz, force increased slowly. It increased further when the rate changed to 1.0 Hz. At L_{max}, resting force was about one third of developed force (Table I). At greater lengths, resting force increased rapidly and developed force declined.

Group 1

The effect of stimulation frequency on developed force was examined over the range 0.5 to 2.5 Hz (pH 7.4, 34°C, Ca^{2+} concentration 2.5 mM). Maximum contractile force was developed at a frequency of 1 Hz (Fig. 1) with a steady fall as frequency increased.

Group 2

When the effect of pH on developed force (1 Hz, 34°C, Ca^{2+} concentration 2.5 mM) was measured, maximum force was found to develop at pH 7.4 (1.04 ± 0.18 g [± SE]). At the other two pH levels used, force was smaller although the difference was not great (0.88 ± 0.26 g at pH 6.7 and 0.94 ± 0.18 g at pH 7.9).

Group 3

Below 30°C there was a notable and consistent decline in force (Fig. 2). The response at 35°C was greater than at either 30°C or 40°C but the variation was not large over this range.

Group 4

A fairly large increase in force was evident over the range of Ca^{2+} levels from 1.5 to 3.0 mM, half maximum force being reached at about 2.0 mM. Above 3.0 mM a plateau was reached (Fig. 3) that approached a value about 25% higher than that in 2.5 mM Ca^{2+}

Discussion

With the procedure described and the selection criteria outlined, it is possible to obtain reasonably consistent contractile responses from isolated human atrial trabeculae. It is not easy to compare the values we obtained with those of others using human myocardial tissue because a standardized procedure and standardized measurement of contractile force are lacking. Only one study of human myocardium out of 11 reports we surveyed expressed developed tension in normalized units (g/mm^2).[10] Sonnenblick and colleagues[10] had a value of 1.81 ± 1.19 g/mm^2 (± SD) for human papillary muscle, which is about 30% higher than the value we obtained for atrial muscle. Studies using human atria generally involve large atrial samples[1,2] or atrial strips.[8] In such preparations the myocytes would not be parallel and aligned with the axis of force measurement so that maximum developed force would not be reached. Wagner and associates[8] used atrial strips about 1 mm in diameter and reported values of 233 ± 30 g/g dry weight, which would correspond to about 150 mg/mm^2. Large atrial preparations, such as those used by Levy,[1,2] with weights up to 160 mg appear to give muscle forces of up to 2 g, which would correspond to very low tensions expressed either on a g/g basis or as tension per unit area. Gristwood and associates[7] used atrial trabeculae 1.0 ± 0.1 mm in diameter. They did not tabulate results but their figures indicated muscle forces of 0.3 to 1.0 g which are comparable, although lower, than those we measured.

Most of our samples were taken from patients with coronary artery disease. It is not possible to tell to what extent this might have affected the preparations, but we found no clear difference between these preparations and those taken from patients with other heart defects. The specimens seem preferable to those taken soon after death of noncardiac origin. Abraitis and Stropus[11] took atrial strips, which varied in diameter from 1 to 2 mm post mortem. Their recordings indicated a developed force of about 100 mg which would correspond to about 4% of the tension we observed and are certainly much smaller than contractions observed with similar atrial strips taken during operation.[8]

It is not yet possible to define any theoretical expected value for normalized tension development of the myocardial contractile elements although Fabiato[12] obtained a maximum value for "skinned" rabbit myocytes fully saturated with calcium of 11.67 g/mm^2. As he pointed out, only about 20% of this force may be mobilized in a single twitch, which is normally limited by both the Ca^{2+} concentration and the duration of the twitch. The contractile force we recorded is thus at least of the order of magnitude expected from Fabiato's observations.

We have found an optimal frequency of 1 Hz under the conditions used. This could, of course, be different with different external conditions (temperature Ca^{2+} concentration). The optimal frequency appears similar to that observed by Levy,[1] although he did not give a systematic tabulation of results.

The acute effect of pH changes over the range of 6.7 to 7.9 is relatively small. Possibly, the effects of metabolic acidosis would be greater over a longer period since the myocardium has a large intracellular buffering capacity,[13] so it would require some time for an extracellular change to be converted into an intracellular pH shift.

The sharp decline in force at temperatures below 30°C has not been reported previously. It seems surprising since we have not seen a similar fall in developed force in other species. This perhaps warrants further investigation.

The increase in contractile force with increasing Ca^{2+} concentration is typical of the myocardial response seen in other species, such as the dog[14] and rat.[15] As in the case of dog myocardium, it appears that maximum contractile force is only developed at higher Ca^{2+} levels than are normally found in plasma. Rat heart, on the other hand, has a lower Ca^{2+} requirement with half maximum activation at about 0.4 mM Ca^{2+} compared with 2.0 mM found for human atrial muscle under the conditions described in these experiments.

The conditions we chose for the second equilibration period (34°C, 1 Hz, pH 7.4, Ca^{2+} concentration 2.5 mM), on which normalized values are based, are close to those required for maximum force development, although a further exponential type of increase would be given by raising Ca^{2+} to a still higher level.

Isolated trabeculae from discarded surgical specimens appear to provide a useful preparation for study. Under the conditions described here, the expected range of tension development is 1.37 ± 0.09 g/mm^2. The small size of the trabecular preparation has the additional advantage that diffusion distances are small so that the time required for equilibrating the extracellular space with agents such as cardioactive drugs would be minimal. The preparation has great potential for the study of the myocardial response to perioperative events such as perfusion, cardioplegia and pharmacologic manipulations.

We acknowledge the technical assistance of Mrs. R. Ravindra and Mrs. D. Ayres.

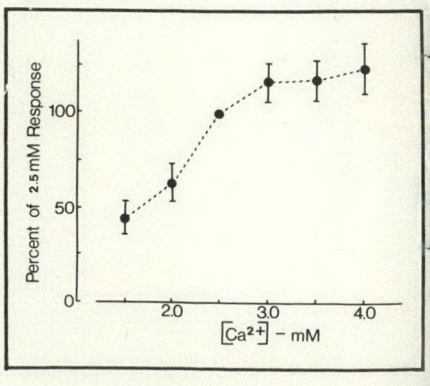

FIG. 3—Calcium concentration–force relation (force at 2.5 mM Ca^{2+} = 100%) and standard error (vertical lines) for 12 trabeculae; pH 7.4, frequency 1 Hz, 34°C.

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ACTION

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INDICATIONS AND CLINICAL USES

CEFOBID (cefoperazone sodium) may be indicated for the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

LOWER RESPIRATORY TRACT INFECTIONS caused by *Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Streptococcus pyogenes, Klebsiella* species (including *Klebsiella pneumoniae), Pseudomonas aeruginosa, Escherichia coli, Proteus mirabilis*, indole-positive *Proteus* species and *Enterobacter* species.

URINARY TRACT INFECTIONS caused by *Escherichia coli, Pseudomonas aeruginosa, Enterobacter* species, Klebsiella species, Enterococcus, *Proteus mirabilis, Staphylococcus aureus, Staphylococcus epidermidis* and indole-positive *Proteus* species.

Due to the nature of the underlying conditions which usually predispose patients to *Pseudomonas* infections of the lower respiratory and urinary tracts, a good clinical response accompanied by bacterial eradication may not be achieved despite evidence of *in vitro* sensitivity.

ACUTE BILIARY TRACT INFECTIONS ASSOCIATED WITH CHOLECYSTITIS OR CHOLANGITIS caused by *Escherichia coli.*

SEPTICEMIA caused by *Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus agalactiae, Escherichia coli* and *Klebsiella* species.

WOUND INFECTIONS (SURGICAL AND TRAUMATIC) caused by *Staphylococcus aureus, Streptococcus pyogenes* and *Pseudomonas aeruginosa.*

GYNECOLOGICAL INFECTIONS (SUCH AS PELVIC INFLAMMATORY DISEASE AND ENDOMETRITIS) caused by *Streptococcus agalactiae, Neisseria gonorrhoeae, Escherichia coli, Bacteroides* species (including *Bacteroides fragilis), Peptococcus* species and *Peptostreptococcus* species.

Specimens for bacteriologic culture should be obtained prior to therapy in order to identify the causative organism and to determine its susceptibility to CEFOBID (cefoperazone sodium). Therapy may be instituted before results of susceptibility testing are known; however, modification of the treatment may be required once these results become available.

CONTRAINDICATIONS: CEFOBID (cefoperazone sodium) is contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

WARNINGS: Before therapy with CEFOBID (cefoperazone sodium) is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins or other drugs. CEFOBID (cefoperazone sodium) should be administered with caution to penicillin-sensitive patients or to any patient who has demonstrated some form of allergy, particularly to drugs. If an allergic reaction to CEFOBID (cefoperazone sodium) occurs, discontinue administration of the drug and treat the patient with the usual agents (e.g. epinephrine, antihistamines, pressor amines or corticosteroids).

Pseudomembranous colitis has been reported to be associated with the use of CEFOBID (cefoperazone sodium). Therefore, in those patients administered CEFOBID (cefoperazone sodium) who develop diarrhea, it is important to consider such a diagnosis.

Treatment with broad-spectrum antibiotics, including CEFOBID (cefoperazone sodium), alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.

Mild cases of colitis may respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated. When the colitis is not relieved by the discontinuance of CEFOBID (cefoperazone sodium) or when it is severe, consideration should be given to the administration of oral vancomycin.

PRECAUTIONS

General: The concomitant administration of aminoglycosides and some cephalosporins has caused nephrotoxicity. Although transient elevations of BUN and serum creatinine have been observed, there is no evidence that CEFOBID (cefoperazone sodium) when administered alone causes significant nephrotoxicity. However, the effect of administering CEFOBID (cefoperazone sodium) concomitantly with aminoglycosides is not known.

CEFOBID (cefoperazone sodium) is excreted in both the bile and urine. In normal volunteers, 19 to 41% of the dose is excreted in the urine, the remainder being excreted by the hepato-biliary system. The serum half-life of CEFOBID (cefoperazone sodium) is usually prolonged and urinary excretion of the drug increased in patients with hepatic disease and/or biliary obstruction. Serum concentrations of cefoperazone should be monitored in these patients treated with doses in excess of 2 grams daily and dosage should be adjusted as necessary.

Because renal excretion is not the main route of elimination of cefoperazone, adult patients with renal failure usually require no adjustment in dosage when daily doses of 2 to 4 grams (1 to 2 grams every 12 hours) are administered. If higher doses of CEFOBID (cefoperazone sodium) are used, serum concentrations of cefoperazone should be monitored. If there is evidence of accumulation, dosage should be decreased accordingly.

In one study in patients with chronic renal failure, the half-life of CEFOBID (cefoperazone sodium) was reduced from 4.17 to 1.67 hours during hemodialysis. Thus, dosing should be scheduled to follow a dialysis period.

In patients with both hepatic dysfunction and renal impairment, the initial dosage of CEFOBID (cefoperazone sodium) should not exceed 1 to 2 grams daily and serum concentrations of cefoperazone should be monitored closely.

Vitamin K deficiency has occurred in a few patients treated with CEFOBID (cefoperazone sodium). The mechanism is most probably related to the suppression of gut flora which normally synthesizes this vitamin. Those at risk include patients with poor diet or malabsorption states (e.g. cystic fibrosis) and patients on prolonged intravenous alimentation regimens. Prothrombin time should be monitored in these patients and exogenous vitamin K administered as indicated.

A reaction characterized by flushing, sweating, headache, and tachycardia has been reported when alcohol is ingested during and as late as the fifth day after CEFOBID (cefoperazone sodium) administration. Patients should be cautioned concerning ingestion of alcoholic beverages in conjunction with administration of CEFOBID (cefoperazone sodium). For patients requiring artificial feeding orally or parenterally, solutions containing ethanol should be avoided.

CEFOBID (cefoperazone sodium) should be administered with caution to individuals with a history of gastrointestinal disease, particularly colitis.

Overgrowth of nonsusceptible organisms may occur during prolonged use of CEFOBID (cefoperazone sodium). Patients should be observed carefully during treatment. If superinfection occurs, appropriate measures should be taken.

Drug Laboratory Test Interactions

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution.

Pregnancy: The safety of CEFOBID (cefoperazone sodium) in pregnancy has not been established. The use of CEFOBID (cefoperazone sodium) in pregnant women requires that the likely benefit from the drug be weighed against the possible risk to the mother and fetus.

Reproduction studies have been performed in mice, rats and monkeys at doses up to 10 times the human dose and have revealed no evidence of impaired fertility or teratogenic effects due to cefoperazone sodium. Animal reproduction studies, however, are not always predictive of human response.

Nursing Mothers: Cefoperazone is excreted in low concentration (0.4 to 0.9 μg/mL) in human milk. Caution should be exercised when CEFOBID (cefoperazone sodium) is administered to a nursing mother.

Children: The safety and efficacy of CEFOBID (cefoperazone sodium) in children have not been established.

ADVERSE REACTIONS

Hypersensitivity: Maculopapular rash, urticaria, pruritis, eosinophilia, drug fever.

Hematology — Decreases in hemoglobin and/or hematocrit have occurred. Slight decreases in neutrophil count have been reported, and reversible neutropenia may occur with prolonged administration. Transient eosinophilia has occurred. Hypoprothrombinemia has been observed. Some individuals have developed positive direct Coombs' test during treatment.

Liver — Transient elevations in SGOT, SGPT and alkaline phosphatase levels have been noted. One patient with a history of liver disease developed significantly elevated liver function enzymes during therapy with CEFOBID (cefoperazone sodium). Clinical signs and symptoms of nonspecific hepatitis accompanied these increases. After CEFOBID (cefoperazone sodium) therapy was discontinued, the patient's enzymes returned to pre-treatment levels and the symptomatology resolved.

Kidney — Transient elevations of blood urea nitrogen and serum creatinine have been noted.

Gastrointestinal — Altered bowel habits (loose stools or diarrhea) have been reported. Most of these events have been mild or moderate, but some have been severe. In all cases, these symptoms responded to symptomatic therapy or ceased when cefoperazone therapy was stopped. Nausea and vomiting have been reported rarely.

Pseudomembranous colitis has been reported rarely in patients administered CEFOBID (cefoperazone sodium). Symptoms of pseudomembranous colitis can appear during or for several weeks subsequent to antibiotic therapy.

Disulfiram-like Reaction

Disulfiram-like reactions have been reported when alcohol was ingested during and as late as the fifth day after CEFOBID (cefoperazone sodium) administration.

Central Nervous System — Headache and dizziness occur rarely.

Local Reactions — CEFOBID (cefoperazone sodium) is well tolerated following intramuscular administration. Occasionally, transient pain may follow administration by this route. When CEFOBID (cefoperazone sodium) is administered by the intravenous route, some patients develop phlebitis at the site of administration.

Other — Diaphoresis/chills

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Since no case of overdosage has been reported to date with CEFOBID (cefoperazone sodium), no specific information on symptoms or treatment of overdosage is available. Treatment should be symptomatic.

Hemodialysis is not effective in the removal of cefoperazone.

DOSAGE AND ADMINISTRATION

DOSAGE

CEFOBID (cefoperazone sodium) may be administered intravenously or intramuscularly.

Dosage and route of administration should be determined by severity of infection, susceptibility of the causative organism, and condition of the patient.

Adult

The recommended daily dose of CEFOBID (cefoperazone sodium) is 2 to 9 grams administered in equally divided doses every 8 to 12 hours (See table below). The usual duration of treatment is 7 to 14 days.

Adult Dosage

Type of Infection	Daily Dose	Frequency and Route
Mild to moderately severe infections such as pneumonia, acute urinary tract infection, wound infection	2 to 4 grams	1 to 2 grams every 12 hours I.M. or I.V.
Severe infections or infections caused by less sensitive organisms	4 to 8 grams	2 to 4 grams every 12 hours I.V.
Infections commonly requiring antibiotics in higher dosage (e.g. septicemia and life-threatening infections)	9 grams	3 grams every 8 hours I.V.

The maximum adult daily dose should not exceed 9 grams.

For infections caused by *Streptococcus pyogenes*, therapy should be continued for at least 10 days.

Impaired Renal Function

Because renal excretion is not the main route of elimination of cefoperazone, adult patients with renal failure usually require no adjustment in dosage when daily doses of 2 to 4 grams (1 to 2 grams every 12 hours) of CEFOBID (cefoperazone sodium) are administered. If higher doses of CEFOBID (cefoperazone sodium) are used, serum concentrations of cefoperazone should be monitored. If there is evidence of accumulation, dosage should be decreased accordingly. For patients whose glomerular filtration rate is less than 18 mL/min or whose serum creatinine level is greater than 3.5 mg/dL, the maximum CEFOBID (cefoperazone sodium) dosage should be 4 grams per day.

In patients undergoing hemodialysis, dosing should be scheduled to follow a dialysis period.

Hepatic Disease and Biliary Obstruction

The serum half-life of cefoperazone is increased 2 to 4 fold in patients with hepatic disease and/or biliary obstruction. Serum concentrations of cefoperazone should be monitored in patients treated with doses in excess of 2 grams daily and dosage should be adjusted as necessary.

Hepatic Dysfunction and Renal Impairment

In patients with both hepatic dysfunction and concomitant renal impairment, the initial dosage of CEFOBID (cefoperazone sodium) should not exceed 1 to 2 grams daily and serum concentrations of cefoperazone should be closely monitored.

Children

The safety and efficacy of CEFOBID (cefoperazone sodium) in children have not been established.

ADMINISTRATION

Intramuscular:

CEFOBID (cefoperazone sodium) should be administered by deep intramuscular injection into a large muscle mass such as the gluteus maximus or anterior thigh. The maximum dose of CEFOBID (cefoperazone sodium) should be two (2) grams.

Intravenous:

Direct Intravenous (bolus) Injection: The reconstituted solution should be injected slowly over a period of **no less than three (3) minutes.** The maximum dose of CEFOBID (cefoperazone sodium) should be two (2) grams.

Intermittent Intravenous Infusion: The reconstituted solution may be infused over a period of 15 minutes to 1 hour through the tubing of an administration set while any of the intravenous solutions (See Solutions for I.V. Infusion) are being infused. During infusion of the solution containing CEFOBID (cefoperazone sodium), it is desirable to temporarily discontinue administration of the other solution.

Continuous Intravenous Infusion: CEFOBID (cefoperazone sodium) may also be administered over a longer period of time.

Note: If therapy with CEFOBID (cefoperazone sodium) is carried out in combination with an aminoglycoside antibiotic, each should be administered at different sites because of a physical incompatibility. An aminoglycoside should not be mixed with CEFOBID (cefoperazone sodium) in the same container.

PHARMACEUTICAL INFORMATION

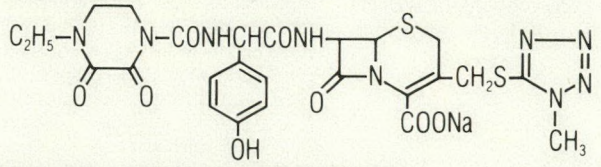
CHEMISTRY

Trade Name: CEFOBID

Proper Name: Cefoperazone sodium

Chemical Name:

Sodium (6R,7R)-7-[(R)-2-(4-ethyl-2,3-dioxo-1-piperazinecarboxamido)-2-(p-hydroxyphenyl) acetamido]-3 [[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0] oct-2-ene-2-carboxylate



Molecular Formula: $C_{25}H_{26}N_9O_8S_2Na$ **Molecular Weight:** 667.65

Description:

Cefoperazone sodium is a white powder, soluble in water, sparingly soluble in methanol, poorly soluble in ethanol, and insoluble in ethyl ether, acetone, chloroform, or n-hexane.

Composition:

CEFOBID vials contain cefoperazone sodium (expressed in terms of free acid). The sodium content of each gram of CEFOBID is approximately 34 mg (1.5 mEq sodium ion). The pH of a 25% (w/v) solution is 4.5 to 6.5 and the solution is colorless to straw yellow depending on the concentration.

RECONSTITUTION

For Intramuscular Use:

Solution for Reconstitution

Sterile Water for Injection
or, if required
Bacteriostatic Water for Injection
0.5% Lidocaine Hydrochloride Injection

Reconstitute as follows:

Vial Size (g)	Volume to be Added to Vial (mL)	Approximate Available Volume (mL)	Approximate Average Concentration (mg/mL)
1.0	3.5	4.0	250
2.0	7.0	8.0	250

Shake well until dissolved. Solutions should be allowed to stand after reconstitution to allow any foaming to dissipate in order to permit visual inspection for complete solubilization. Vigorous and prolonged agitation may be necessary to solubilize CEFOBID (cefoperazone sodium).

For Intravenous Use:

Solutions for Reconstitution and Dilution

Sterile Water for Injection
or, if required
Bacteriostatic Water for Injection

Reconstitute as follows:

Vial Size (g)	Volume to be Added to Vial (mL)	Approximate Available Volume (mL)	Approximate Average Concentration (mg/mL)
1	9.5	10.0	100
2	19.0	20.0	100

Shake well until dissolved. The prepared solution may be further diluted to the desired volume with any of the solutions for I.V. infusion listed below.

For direct intravenous (bolus) injection: Reconstitute as directed above.

For intermittent intravenous infusion: Reconstitute as directed above.

For continuous intravenous infusion: Reconstitute with Sterile Water for Injection. The reconstituted solution may be added to an appropriate intravenous bottle/bag containing any of the solutions for I.V. infusion listed below:

Solution for I.V. Infusion

5% Dextrose Injection (USP)
5% Dextrose and Lactated Ringer's Injection
5% Dextrose and 0.9% Sodium Chloride Injection (USP)
5%Dextrose and 0.2% Sodium Chloride Injection (USP)
10% Dextrose Injection (USP)
Lactated Ringer's Injection (USP)
0.9% Sodium Chloride Injection (USP)
Normosol® M and 5% Dextrose Injection
Normosol® R

Stability of Solutions

Storage:

Reconstituted solutions for intramuscular injection should be used within 24 hours if kept at room temperature, or 72 hours if stored under refrigeration (5°C).

Reconstituted solutions for I.V. injection or infusion should be used within 24 hours if kept at room temperature, or 72 hours if stored under refrigeration (5°C).

Incompatibility

CEFOBID (cefoperazone sodium) should not be added to blood products, protein hydrolyzates, or amino acids. CEFOBID (cefoperazone sodium) should not be mixed together with an aminoglycoside.

DOSAGE FORMS

Availability:

CEFOBID (cefoperazone sodium) is available as a lyophilized powder:

1.0g vial — cefoperazone 1.0 g as sodium salt
2.0g vial — cefoperazone 2.0 g as sodium salt

Storage

CEFOBID (cefoperazone sodium) should be stored protected from light and refrigerated (2 to 8°C).

References:

1. Official product monograph.
2. Data on file.

*Prepared by Pfizer Canada Inc. (R.U.)
Pfizer Inc. TM Owner.

Pfizer Canada Inc.
Kirkland, Quebec H9J 2M5

PAAB
CCPP

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NICHOLAS M. NEWMAN, MD;* JOHN V. FOWLES, MD, FRCS[C]†

A Case of "Trigger Toe"

"Triggering" of the toes, in which local tendon hypertrophy prevents the smooth movement of the tendon, has been described as a problem more theoretical than real and only three cases have been reported.

The authors report a case of partial tethering of the flexor hallucis longus tendon just distal to the medial malleolus in a 28-year-old jogger who had painful triggering of the great toe on plantar flexion of the ankle and great toe.

Division of the flexor hallucis longus tendon pulley distal and posterior to the medial malleolus cured the patient.

Le problème des orteils à ressort a été jugé comme un problème plus théorique que réel. Le gros orteil est rarement affecté.

Les auteurs décrivent un cas d'orteil à ressort dû à un blocage partiel du tendon du long fléchisseur du gros orteil, blocage distal à la malléole interne. La patiente est âgée de 28 ans. Elle fait de la course à pied et souffre depuis 5 ans de symptômes progressifs et douloureux reliés à l'orteil à ressort.

Une section chirurgicale de la poulie du tendon du long fléchisseur du gros orteil distale et postérieure à la malléole interne a résolu le problème de ressort.

Localized tendon hypertrophy, usually of inflammatory or traumatic origin, can obstruct the smooth gliding of the tendon through its pulley, producing a "triggering" sensation as the obstruction is overcome. Typically, the first annular component of the digital flexor sheath in the hand is the site of the obstruction. Only rarely has "triggering" been reported in the foot.[1-3] We report here the case of a patient with stenosing tenovaginitis of the sheath of the flexor hallucis longus.

Case Report

A 28-year-old woman, who daily jogged 2 miles, noticed a painless snapping sensation in the left great toe over a 5-year period. One year previously she had sprained her left ankle while skiing, and after this she had intermittent pain distal and posterior to the medial malleolus associated with a snapping sensation at the first metatarsophalangeal joint. Persisting symptoms, including inability to jog, led the patient to seek medical advice 1 year after her skiing injury.

On physical examination there was no deformity or tenderness, and passive movements of the toes, foot and ankle were normal and painless. Following active plantar flexion of the ankle and great toe, attempted active dorsiflexion of the great toe caused a clawing deformity with further interphalangeal joint flexion. This deformity could be overcome actively and produced an audible and palpable "snapping" as the interphalangeal joint returned to neutral. The snapping could be felt along the course of the flexor hallucis longus tendon both distal to the medial malleolus and on the plantar aspect of the great toe. We made the clinical diagnosis of stenosing tenovaginitis of a pulley of the flexor hallucis longus. This tendon passes through two flexor sheaths, a proximal sheath behind the talus and beneath the sustentaculum tali and a distal one beneath the neck and head of the first metatarsal[4] (Fig. 1).

The flexor hallucis longus was explored under local anesthesia to permit active triggering during operation. There was no abnormality at the metatarsophalangeal level. Through a second incision, distal and posterior to the medial malleolus, the proximal pulley was approached by reflecting anteriorly the posterior tibial nerve while preserving its calcaneal branches. A fusiform thickening of the flexor hallucis longus was observed just proximal to this pulley which was also very thick. There was no dislocation or obvious laceration of the tendon and the synovium was not hypertrophied. Longitudinal sectioning of this flexor sheath eliminated the triggering. Six months after operation the patient was free of pain and symptoms.

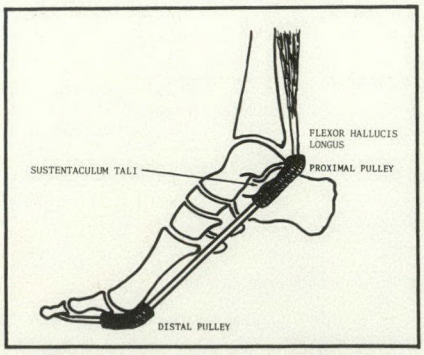

FIG. 1—Path of flexor hallucis longus tendon and position of proximal and distal flexor tendon sheaths.

Discussion

The flexor hallucis longus muscle arises from the inferior two thirds of the posterior surface of the fibula and from the interosseous membrane.[4] The position of its tendon is maintained by two pulleys, a proximal one beneath the sustentaculum tali and a distal one beneath the first metatarsal. The muscle is particularly important for pushoff in running and has a function analogous to the Achilles tendon for the ballet dancer *en pointe*.[5]

The triggering phenomenon is most common in the hand at the level of the metacarpal head. It may be congenital or related to inflammatory disease, particularly rheumatoid tenosynovitis. Nonspecific tenosynovitis or tendon injury, or partial tendon rupture causing tendon irregularity as the ruptured fibres retract, may also produce triggering.[6] While tendinitis of the flexor hallucis longus is well recognized, particularly in ballet dancers, triggering is so rare that only three cases have been reported, two of them in ballet dancers;[1,3,5] Jahss[7] even doubted its existence.

The site of triggering in our patient could not be determined preoperatively because the triggering snap was transmitted along the whole length of the tendon. In retrospect, exploration of the metatarsophalangeal pulley was unnecessary. The cause of the localized tendon enlargement was not definitely identified, but since there was no synovitis, partial rupture of central fibres in the tendon as described by Sammarco and Miller[3] seems likely.

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Amphojeloma: Antacid Impaction in a Critically Ill Patient

Patients in the intensive care unit seldom have mechanical small-bowel obstruction, and obstruction due to medication bezoars is even less common. A 65-year-old woman, in the intensive care unit because of septic shock and acute renal failure, had a small-bowel obstruction due to Amphojel concretions. Obstruction from such a cause may be prevented by including non-constipating antacids, stool softeners or sorbitol. Aggressive use of H_2-antagonists to prevent gastrointestinal bleeding in septic patients will reduce the need for orally administered antacids. When obstruction occurs due to antacid concretions, it may be relieved by passing a long intestinal tube, by giving enemas for colonic obstruction or by operation.

Il est peut fréquent qu'un patient soit accueilli aux soins intensifs souffrant d'une obstruction mécanique du grêle, et une obstruction due à un bézoard d'origine médicamenteuse est encore plus rare. Une femme de 65 ans, admise aux soins intensifs en choc septique et en insuffisance rénale aiguë, a présenté une obstruction de l'intestin grêle due à des concrétions d'Amphojel. Une obstruction de ce type peut être prévenue en donnant des anti-acides qui ne provoquent pas de constipation et en administrant une substance capable d'amollir les selles ou du sorbitol. L'utilisation systématique des antagonistes des récepteurs H_2 chez les patients septiques dans le but de prévenir les hémorragies gastro-intestinales va réduire le besoin d'anti-acides oraux. On peut corriger une obstruction intestinale due à des concrétions d'anti-acides en passant un long tube intestinal, en donnant des lavements ou en procédant à une intervention chirurgicale.

From the Intensive Care Unit, Kingston General Hospital, Kingston, Ont.

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Acute renal failure is a common accompaniment of multiple organ failure in critically ill septic patients.[1] These patients are at risk of a major gastrointestinal hemorrhage for a number of reasons, one of which is believed to be prolonged exposure of the gastric mucosa to unopposed gastric acidity.[2] Aggressive medical management of the acute renal failure and gastric acidity involves the use of both H_2-antagonists and antacids. In this setting Amphojel, an aluminum-containing antacid, is ideal because of its high buffering capacity and phosphate-binding characteristics. There are scattered reports in the literature of complications resulting from the use of aluminum-containing antacids in critically ill patients.[3-6] We report a patient with overwhelming sepsis and acute renal failure who had a complete small-bowel obstruction as a result of hardened Amphojel concretions.

Case Report

A 65-year-old woman was known to suffer from alcoholism and long-standing insulin-dependent diabetes. Several operative procedures had been performed including a hysterectomy, bilateral oophorectomy and a cholecystectomy several years before. For 1 year she had had chronic urinary tract infections.

The patient initially presented to a local hospital with a short history of fever, chills, anorexia and drowsiness. She was noted to have foul smelling urine. For 72 hours she had refractory, elevated blood sugar levels and episodes of hypotension and confusion. Her renal function progressively declined so she was transferred to the Kingston General Hospital.

On admission, the patient was disoriented, confused and unable to provide a history. She was markedly obese and had extreme tenderness in the right flank. Vital signs were as follows: temperature 40°C, blood pressure 70/40 mm Hg, respiratory rate 24/min, heart rate 120 beats/min. Her hemoglobin level was 70 g/L, leukocyte count 23 × 10^9/L, platelets 105 × 10^9/L, serum sodium 131 mmol/L, potassium 6.3 mmol/L, chloride 100 mmol/L and carbon dioxide 15 mmol/L. Renal failure was present with a blood urea nitrogen level of 73.19 mmol/L urea and a serum creatinine level of 680 μmol/L. Arterial blood gas measurements made on a partial intake of oxygen of 40% revealed a pH of 7.3, partial pressure of oxygen of 87.2 mm Hg, of carbon dioxide 27.9 mm Hg and a bicarbonate level of 13 mmol/L. Gram staining of the urine showed large numbers of leukocytes and gram-negative bacteria. Subsequent cultures grew *Escherichia coli* from both urine and blood. The patient was stabilized after hemodynamic monitoring lines were placed and broad spectrum antibiotics including tobramycin, clindamycin and erythromycin were given. Dopamine in the range of 4 to 6 μg/kg was given intravenously to support her blood pressure. Computerized tomography disclosed an emphysematous right kidney. Hemodialysis was instituted. This was followed by appreciable upper gastrointestinal bleeding and the patient's hemoglobin level dropped by 30 g/L. Ulcerative esophagitis, antritis, gastritis and a chronic pyloric channel ulcer were seen at endoscopic examination, but no active bleeding was noted. The patient was given cimetidine 300 mg intravenously twice daily and Amphojel 30 mL every hour as necessary through the nasogastric tube to maintain a gastric pH greater than 4.5.

A right radical nephrectomy was carried out 24 hours after admission. Microscopic examination of the specimen disclosed acute pyelonephritis with acute papillary necrosis and diffuse glomerulosclerosis. Two days after operation, the patient was returned to the operating room because of continued bleeding from the incision in the right flank. Frank blood was noted in the peritoneal cavity and a laparotomy was done. Three litres of blood were found in the peritoneal cavity but no abdominal source of bleeding and no perforation were seen in either the stomach or duodenum. There were many dense adhesions and multiple putty-like concretions in the small bowel. Due to the patient's unstable condition these concretions were not removed; preoperative medications including Amphojel were restarted.

Over the following week the patient continued to deteriorate. Her abdomen became grossly distended and markedly tender in all four quadrants. Clinically and radiologically, a small-bowel obstruction was diagnosed. Sepsis was also evident hemodynamically by decreased systemic vascular resistance and increased cardiac output despite appropriate antibiotics. Oliguria remained and the patient required frequent hemodialysis to control the renal failure.

The patient continued to deteriorate; 18 days after admission she was reexplored. There was no focus of infection. However, the small bowel from the ligament of Treitz to the sigmoid colon was filled with rock-hard concretions. The small bowel was grossly dilated in several areas with early ischemia adjacent to the concretions. The adhesions were lysed and through an ileotomy the concretions were removed. An ileostomy and mucous fistula were then formed. The concretions were rock-hard balls of Amphojel mixed with bile. All elements were removed from the bowel. The spleen was incidentally traumatized during this procedure and was removed.

The patient remained in septic shock with an elevated leukocyte count despite adequate antibiotic coverage with amphotericin B. Cultures of the sputum, urine and spleen revealed a pure growth of *Torulopsis glabrata.* She continued to deteriorate and died 30 days after admission of widely disseminated fungal septicemia.

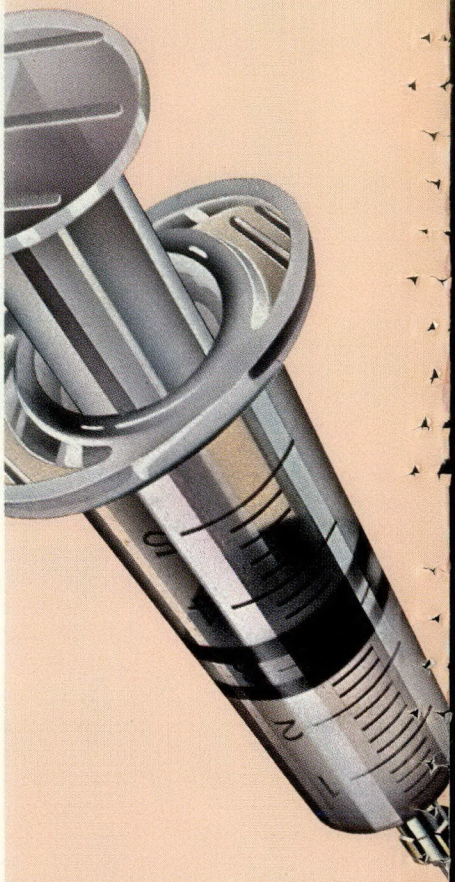
Discussion

Mechanical intestinal obstructions are common in clinical surgical practice. However, impaction of feces or, less commonly, medications, accounts for only 1% to 2% of patients with mechanical intestinal obstruction reviewed in large series.[7] In the intensive care unit, paralytic ileus is more commonly seen due to prolonged sepsis, major trauma or drug administration. It is also recognized that in these patients gastrointestinal hemorrhage can be a major concern.[2] Aggressive medical management with H_2-antagonists such as cimetidine and antacids has been reported to decrease the incidence of gastrointestinal hemorrhage.[8-10] If the patient is also in renal failure, the dosage of the H_2-antagonists is adjusted and the preferred antacid is one that contains aluminum.[1] These antacids are, however, notoriously constipating although they are effective buffers and bind intestinal phosphates, thus reducing the risk of hyperphosphatemia in acute renal failure. Magnesium-containing antacids are generally not used because they may cause magnesium intoxication leading to serious neurologic and cardiovascular effects. Calcium carbonate is also avoided because of the possibility of hypercalcemia.[11] Patients in the intensive care unit receiving aluminum-containing antacids for control of gastric acidity and having episodes of prolonged paralytic ileus and major cardiovascular instability are at risk of medication impaction in the large bowel or, less frequently, the small bowel.

Antacid impaction or medication bezoars have been reported in patients on long-term renal dialysis and those who have undergone renal transplantation. The most complete review was by Welch and associates[6] in which 10 cases of colonic impaction were recorded in 180 transplant patients and those with chronic renal failure over a 6-year period. The impactions were always in the colon. Three patients in their group died. Small-bowel obstruction due to Amphojeloma is exceedingly rare; only three cases have been reported. The mortality for small-bowel obstruction due to antacid impaction is about 50%.

To avoid antacid impaction in critically ill patients, there are several treatment possibilities. First, antacid regimens may be altered to include nonconstipating agents such as magnesium hydroxide, unless it is contraindicated. Second, the use of stool softeners such as Colace and the addition of sorbitol may decrease the constipating effect of aluminum antacids. Gastric acidity may be controlled through the aggressive intravenous administration of H_2-antagonists such as cimetidine; this permits a reduction in the frequency of oral antacid administration. The effectiveness of this therapy in preventing gastrointestinal hemorrhages has been debated.[12] Lastly, proper hydration may soften the mixture of Amphojel and secretions within the small bowel.

When the bowel is obstructed by multiple small-bowel or colonic concretions formed by antacids, several options are available to relieve the obstruction. A long intestinal tube may be used for drainage as well as for the administration of softeners and for cathartics. If the colon is primarily involved, enemas may relieve the impaction. These enemas contain various combinations of Colace, olive oil, trypsin and soap suds. The use of hyperosmolar enemas containing Hypaque have been successful in relieving colonic obstruction in a few patients after transplantation. If all conservative measures fail, operation may be required to decompress the bowel and remove all concretions. Anastomoses should be avoided in the unprepared colon or in the presence of contamination. The preferred procedure is an ileostomy and mucous fistula for right-sided or distal small-bowel impactions. The Hartmann procedure is advocated for more distal impactions. If complications such as colonic perforation occur, the prognosis is particularly poor.



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Early Valve Replacement in Active Infective Endocarditis

Infective endocarditis is associated with a high mortality, but previous studies have suggested that the major complications of the condition might be prevented by early surgery. Of 50 patients treated for infective endocarditis at the Montreal Heart Institute from 1977 to 1982, 30 were treated nonsurgically and the remaining 20 underwent early valve replacement before preoperative antibiotic therapy was completed. Of these 20, 14 had native valve endocarditis and 6 prosthetic valve endocarditis. The organisms involved were *Streptococcus* sp in 11, *Staphylococcus aureus* in 2, gram-negative organisms in 3 and *Candida parapsilosis* in 1. Blood cultures remained negative in three patients. There were three early deaths (15%) following operation and one late death (5%). Infection on implanted prostheses did not recur, but reoperation was required in one patient because of prosthetic dehiscence 7 months after initial implantation. All resected valves displayed evidence of infection. Follow-up was obtained in all survivors. After an average follow-up of 26 months, 12 patients remained in functional class I and 4 in class II (New York Heart Association classification). Early valve replacement has resulted in improved survival of patients with infective endocarditis and is now associated with a low operative mortality and morbidity.

L'endocardite infectieuse s'accompagne d'une forte mortalité. Des études antérieures ont indiqué que les complications majeures de cette maladie pouvaient être évitées par une chirurgie précoce. Sur 50 patients traités pour endocardite infectieuse à l'Institut de cardiologie de Montréal entre 1977 et 1982, 30 ont reçu un traitement médical alors que les 20 autres subissaient un remplacement valvulaire précoce avant la fin d'un traitement antibiotique préopératoire. De ces 20 malades, 14 avaient une endocardite affectant les valvules cardiaques naturelles et 6 une infection de valvule prosthétique. Dans 11 cas, le microorganisme responsable était le *Streptococcus* sp, dans 2 cas *Staphylococcus auréus,* des bactéries gram négatif dans 3 et *Candida parapsilosis* dans 1. Les hémocultures sont demeurées négatives chez trois patients. On a enregistré trois décès (15%) tôt après l'opération et un décès tardif (5%). Il n'y a pas eu de récidive d'infection de prothèse, mais une deuxième opération s'avéra nécessaire chez un patient à cause de la déhiscence d'une valvule prosthétique 7 mois après la pose initiale. Toutes les valvules réséquées ont montré des signes d'infection. Tous les survivants ont fait l'objet d'examens de contrôle. Après une période de surveillance moyenne de 26 mois, 12 patients se maintenaient dans la classe fonctionnelle I et 4 dans la classe II (selon la classification de la New York Heart Association). Un remplacement valvulaire précoce a amélioré la survie des patients atteints d'endocardite infectieuse et cette opération est maintenant liée à un faible taux de mortalité et de morbidité peropératoires.

Despite the availability of many new and potent antimicrobial drugs, infective endocarditis still carries a high mortality, owing to the severe complications of this disease. Previous studies have shown that congestive heart failure and systemic embolism occur frequently and are responsible for more than 75% of the deaths.[1,2] Both complications might be prevented by earlier surgical treatment. Therefore, the proper timing of operation appears to be a major, and still unresolved, issue in the management of this condition. There has been reluctance to recommend early valve replacement in these patients because implantation of a prosthetic device in a septic environment is against well-established surgical principles. However, the poor results from the classic treatment have stimulated interest towards a more aggressive attitude. This paper describes our experience with 20 patients who underwent valve replacement early during the active phase of infective endocarditis.

Patients and Methods

From 1977 to 1982, 50 patients with infective endocarditis were treated at the Montreal Heart Institute. There were 28 cases of native valve endocarditis (half were treated medically) and 22 cases of prosthetic valve endocarditis (16 treated medically). During the same period, 980 patients underwent valve replacement. Among the 22 patients treated for endocarditis of a prosthetic valve, 5 infections occurred early (within 2 months of valve implantation) and 17 late. Of the 30 patients managed by medical treatment alone, 4 (13%) died. Three of them had late prosthetic valve endocarditis. Among the 26 patients in whom the infection was successfully controlled by medical treatment, 7 (23%) underwent delayed operation 2 to 11 months (mean 6 months) after onset of the disease, because of late hemodynamic complications following termination of antibiotic treatment. There were no deaths following delayed valve replacement.

Early valve replacement during the active phase of infective endocarditis was performed in 20 patients. There were 15 men and 5 women aged 18 to 69 years (mean 46 years), 14 with native valve endocarditis and 6 with late prosthetic valve endocarditis. In the 14 patients with endocarditis of a native valve, the preexisting valvulopathy was rheumatic in 8, myxoid degeneration in 4 and a bicuspid aortic valve in 2 patients. The aortic valve was involved in seven patients, the mitral in two and both valves in five cases. In the other six patients, a mitral prosthesis was infected in four, an aortic prosthesis in one and both aortic and mitral prostheses in one patient. In 9 of the 20 cases, the site of entry of the infection was

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unknown. A dental infection was responsible for six cases, a urinary infection was the cause in three, and otitis and skin infection were responsible in one patient each. There were no cases of infective endocarditis secondary to drug addiction in our series. Responsible microorganisms are shown in Table I. Active infection was evident on pathologic examination of resected natural or prosthetic valves in all patients, most frequently vegetations (Table II). Following surgery, the specific antimicrobial therapy was continued until treatment had lasted for 6 weeks, including preoperative treatment.

Findings

Preoperative Management

Preoperative investigation included echocardiography in 18 patients (vegetations were indicated in 5), gallium scanning in 6 patients with two positive tests and cardiac catheterization in 5 patients. Indications for hemodynamic studies were double-valve involvement in three and a left-to-right shunt in one patient and for coronary angiography in one patient with previous angina. Antibiotics were selected according to in-vitro sensitivity and administered intravenously. None of these patients completed a full 6-week course of antibiotic therapy before they underwent operation. The duration of treatment preoperatively ranged from 1 to 40 days (average 21 days) (Fig. 1). Early valve replacement was performed because of the sudden appearance or progression of congestive heart failure in 15 patients, resistance to antibiotic treatment as evidenced by persisting fever after 3 weeks of treatment in 3 and major systemic embolism in 2 patients. Two of the patients were in septic shock preoperatively.

Surgical Treatment

The aortic valve was replaced in seven patients (35%), the mitral valve in four (20%) and both valves were replaced in nine patients (45%). In addition, two patients underwent closure of a ventricular septal defect caused by a fistula from aortic valve endocarditis and one patient had coronary bypass grafting in addition to mitral valve replacement. A bioprosthesis was implanted in 17 patients and a mechanical valve in 3. Cold potassium cardioplegia and pericardial irrigation were used to protect the myocardium during operation in all patients. After operation, complete atrioventricular block developed in two patients and a permanent pacemaker had to be implanted.

Postoperative Results and Follow-up

There were three early deaths (within 30 days), from uncontrollable hemorrhage in two patients and from acute renal failure in one. Two patients (14%) in the native valve group died and one (17%) in the prosthetic valve group. There was one late death 2 months postoperatively from intractable arrhythmias. All four deaths occurred in patients who underwent complex surgical procedures (double-valve replacement in two, aortic valve replacement and closure of ventricular septal defect in one and mitral valve replacement associated with coronary bypass grafting in one).

All 16 survivors were available for follow-up, 12 to 60 months after operation (mean 26 months). There were no cases of reinfection of implanted prostheses in our series. One patient underwent reoperation because of massive dehiscence of a mitral valve prosthesis 7 months after initial implantation for fungal infective endocarditis. Antifungal treatment was started preoperatively; amphotericin B was given intravenously for 18 days and flucytosine given orally for 4 days. Both drugs were discontinued on the fourth postoperative day because of rapidly progressive renal failure. A loud mitral systolic murmur and severe congestive heart failure developed. At reoperation, the mitral prosthesis was found to be torn from the annulus at three different sites but there was no evidence of reinfection. The prosthesis was replaced after scrubbing the endocardium with iodine solution. All cultures taken at reoperation were negative. The patient showed no signs of recurrent infection following operation and he remains well 36 months later. At last follow-up, 12 of the 16 patients were in the New York Heart Association functional class I and 4 in class II. An aortic diastolic murmur was noted in 2 of 13 pa-

Table II—Pathologic Findings on Resected Valves

Pathologic feature	No.
Vegetations	16
Abscess	6
Leaflet perforation	4
Fistula of sinus of Valsalva	2
Ruptured chordae	1

Table I—Organisms Responsible for Infective Endocarditis in 20 Patients Treated Surgically*

Organism	No.	%
Streptococcus	11	55
viridans group	9	
faecalis	1	
Peptostreptococcus	1	
Staphylococcus aureus	2	10
Gram-negative organisms	3	15
Haemophilus influenzae	1	
Acinetobacter calcoaceticus	1	
Actinobacillus actinomycetem-comitans	1	
Fungus: *Candida parapsilosis*	1	5

*In 3 patients (15%) no organisms were cultured.

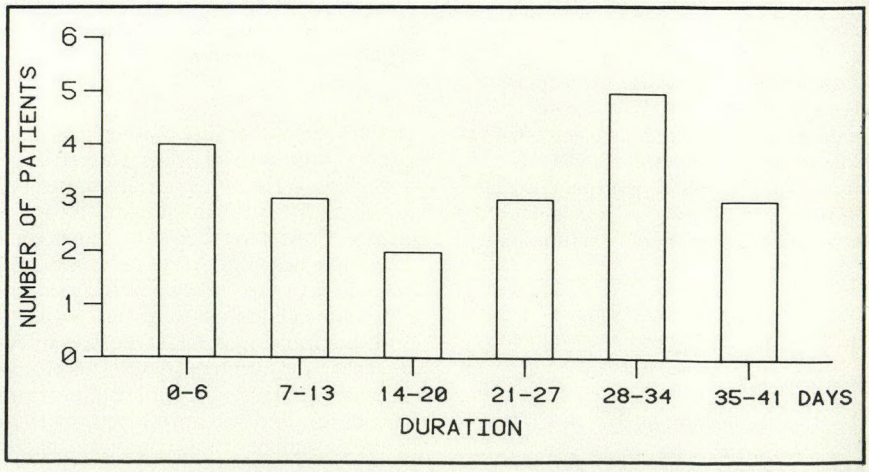

FIG. 1—Duration of preoperative antibiotic treatment (mean 21 days, range from 1 to 40 days) in 20 patients who underwent early valve replacement for infective endocarditis.

tients with an aortic prosthesis, and a mitral systolic murmur in 1 of 10 patients with a mitral prosthesis. Although hemodynamic studies were not performed, none of these regurgitation murmurs appeared to be clinically important.

Discussion

All patients who underwent surgical treatment in our series presented with definite infective endocarditis as defined in the classification of Pelletier and Petersdorf,[3] since evidence of active valve infection was demonstrated on histologic examination in all cases. The indications for and timing of valve replacement in the treatment of infective endocarditis are not yet well defined. Before 1977, the mortality from infective endocarditis was high. Before 1970 at the Montreal Heart Institute, only 67% of patients survived the acute phase of infection and in a second series of patients treated between 1969 and 1977, the overall mortality was 44%, even though more patients were treated surgically.[1,2] Since 1977, the mortality from this disease has decreased markedly to 14% (13% in the nonsurgical group and 15% in the surgical group). Besides the improvements in antimicrobial drugs available and in the surgical and myocardial protection techniques, earlier valve replacement during the course of the disease has played a major role in improving survival. Death results from a major complication, which could have been prevented by earlier surgical treatment in 75% to 90% of cases.[1-3] Comparing the results of nonsurgical and surgical treatments of infective endocarditis, Richardson and associates[4] found a significant difference in the respective mortality rates; they were 44% and 14% for native valve endocarditis, and 75% and 43% for prosthetic valve endocarditis. They therefore recommended early valve replacement when signs of progressive heart failure develop, particularly with aortic valve endocarditis, or if systemic embolization occurs.

Few series of early valve replacement during the active phase of infective endocarditis have been reported (Table III[4-12]). Among 431 patients collected from 10 studies (including the present one) since 1976, there has been a progressive decline in early mortality, which ranged from 18% to 37% between 1976 and 1980 to 16% or less since 1981. In most series, prosthetic valve endocarditis resulted in a higher surgical mortality than native valve disease, but the difference was small in our patients.

Although inserting a prosthesis in a septic environment is against generally recognized surgical principles, our experience and that of others[4,8,12] indicate that the risk of reinfection of the implanted prosthesis is minimal. We have had no case of recurrent infection of a prosthesis following operation and only one case of dehiscence; this required reoperation. Others reported similar results, with reoperation rates ranging from 5% to 14% (Table III). In only one small series was there a high reoperation rate — 33%.[7]

While the organism responsible for the endocarditis can be identified in most patients, the site of entry of infection remains unknown in almost half. When it is known, dental and urinary tract infections or manipulations are most often involved. Improved prophylactic treatment in patients at risk should decrease the incidence of endocarditis secondary to these well-established causes. Contrary to the experience of most others, we have had no cases of right heart infective endocarditis and none of our cases was related to drug addiction.

Echocardiography is a useful noninvasive method for detecting valvular vegetations.[11,13,14] In our series, using either the M-mode or two-dimensional echocardiography, vegetations were shown in only 28% of the patients. Thus, a diagnosis of infective endocarditis cannot be excluded on the basis of a negative echocardiogram. Cardiac catheterization is not helpful for diagnosis and is seldom indicated in these patients, except when involvement of more than one valve is suspected or when coronary angiography is necessary to investigate concomitant coronary artery disease.

Our results are similar to those of Richardson and associates[4] and confirm their conclusion that patients with infective endocarditis should undergo valve replacement early during the course of treatment if congestive heart failure progresses or systemic embolization occurs, regardless of the infective state. This more aggressive attitude has resulted in a marked decline in mortality. However, early prosthetic valve endocarditis still carries a high mortality whether treated surgically or nonsurgically.[4,15] In the present study, five patients were considered to have had early prosthetic valve endocarditis (0.5% of all patients who had valve replacement between 1977 and 1982). All responded to medical treatment. Prevention of this catastrophic complication is the major consideration and the prophylactic regimen used in our patients, which includes skin cleansing with chlorhexidine 0.05% solution and intravenous administration of ampicillin and cloxacillin 1 g every 6 hours for 4 days, starting just before operation, appears to be effective. In addition, special care is given to detection of dental problems or of any active infection preoperatively.

The late results also justify our present attitude, since after an average follow-up of more than 2 years there has been no late prosthetic reinfection and only one valve dehiscence. At follow-up, prosthetic regurgitation murmurs were found in three other patients, but in only one of these was the murmur greater than grade 2/6, and all three patients remained asymptomatic with no evidence of a hemodynamically important regurgitation. However, these patients must be followed up carefully for at least 2 years following operation to detect signs of reinfection or of substantial paravalvular leak. Lau and colleagues[9] have stressed the importance of carrying out complete débridement of the annulus and of removing all necrotic tissue at operation; if the remaining annulus is friable, stitches reinforced with Teflon pledgets should be used. Postoperatively, the antibiotic regimen is determined by the in-vitro sensitivity of the organism involved and is maintained for a minimum of 2 weeks and up to 6 weeks.

Table III—Results of Early Valve Replacement for Infective Endocarditis Reported in the Literature

Authors	No. of patients	Early mortality, %			Reoperation, %
		NVE	PVE	Mean	
Stinson and colleagues, 1976[5]	44	30	24	27	–
Boyd and colleagues, 1977[6]	54	13	57	19	5
Richardson and colleagues, 1978[4]	116	14	43	22	11
Wilson and colleagues, 1978[7]	11	18	–	18	33
Young and colleagues, 1979[8]	30	37	–	37	5
Lau and colleagues, 1981[9]	26	13	–	13	12
Prager and colleagues, 1981[10]	14	0	–	0	14
Lewis and colleagues, 1982[11]	94	14	33	16	6
Symbas and colleagues, 1982[12]	22	9	–	9	5
Present study	20	14	17	15	5
Total/mean, 1976–83	431	17	35	19	11

NVE = native valve endocarditis, PVE = prosthetic valve endocarditis.

Conclusions

Our results lead us to recommend ear-

ly valve replacement during the treatment of infective endocarditis if congestive heart failure progresses, major systemic embolization occurs or if the patient does not respond to medical treatment. Operation should not be postponed in order to complete the antibiotic treatment, since in our experience late complications due to prosthetic reinfection or dehiscence are uncommon and do not justify the greater risk of major systemic complications from delaying definitive surgical treatment.

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DENNIS F. PITT, MD, FRCS[C], FACS

Management of Gangrene in Diabetic Extremities

The long-term complications of diabetes mellitus occur despite insulin therapy. One of these complications is gangrene of an extremity which is a prime cause of morbidity and mortality in diabetic patients. Peripheral occlusive vascular disease frequently underlies the gangrene and this challenges the surgeon to revascularize the limb and to limit the amputation to the gangrenous tissue. The author describes six diabetic patients with gangrene of an extremity treated at the Riverside Hospital in Ottawa to illustrate how this condition may be managed by revascularization with no amputation or with conservative amputation and débridement. Major amputation was avoided in all six patients.

Les complications à long terme du diabète sucré surviennent malgré l'insulinothérapie. La gangrène d'un membre représente une de ces complications; elle est une cause importante de morbidité et de mortalité chez le patient diabétique. La maladie vasculaire oblitérante périphérique est souvent sous-jacente à cette gangrène et ceci incite le chirurgien à revasculariser le membre et à limiter l'amputation au tissu gangréneux. L'auteur décrit six cas de gangrène des membres chez des patients diabétiques qui ont été traités à l'Hôpital Riverside d'Ottawa afin d'illustrer comment cette maladie peut être traitée par revascularisation sans amputation ou avec une amputation conservatrice et débridement. Une amputation majeure a été évitée chez les six patients.

Gangrene is a major complication of diabetes mellitus and contributes appreciably to the morbidity and mortality and to the health-care costs of these patients.[1] The diabetic extremity is susceptible to infection, neuropathy and arterial occlusive disease, which potentiate each other and cause gangrene.[2] Because accelerated atherosclerosis of medium and large vessels is more important than microvascular disease in the etiology of gangrene,[3] surgeons are now able to revascularize and salvage the limbs of many diabetic patients. Often clinicians do not consider revascularization of diabetic extremities with gangrene and even refer these patients to orthopedic surgeons for major amputation or to plastic surgeons for radical débridement rather than to a surgeon who can revascularize the extremity and limit the tissue loss to that which is already dead. A recent major textbook of medicine[1] fails to mention revascularization in its discussion of gangrene in diabetics.

Between March 1981 and March 1983, six diabetic patients with gangrene of an extremity were referred to me at the Riverside Hospital in Ottawa. In all six patients major amputation was avoided by revascularization with or without conservative amputation.

Case Reports

Case 1

A 76-year-old man with insulin-dependent diabetes mellitus had painful gangrene of his entire right fifth toe with erythema and edema of the adjacent foot. The rest of the foot was warm and pain-free with normal sensation; he had no history of claudication or rest pain. The popliteal pulse was present but the pedal pulses were absent. Doppler blood pressure in the posterior tibial artery was 100 mm Hg systolic and the brachial blood pressure was 180 mm Hg systolic. Transmetatarsal amputation of the fifth toe failed to heal and the gangrene spread to involve the fourth and third toes. Angiograms showed a large patent posterior tibial artery with proximal occlusion (Fig. 1). An autogenous reversed saphenous vein graft was inserted from the superficial femoral artery to the posterior tibial artery (Fig. 2). The third and fourth toes were amputated at the transmetatarsal level and the foot healed. The patient had no further trouble with his foot. It was pain-free and fully weight bearing until his death 18 months later.

Comment.—Angiography should be done before any major amputation. If the

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revascularization of the posterior tibial artery had been done before the initial amputation, the patient would have lost only one toe and would have been out of hospital 2 months earlier.

Case 2

While vacationing in Florida, a 70-year-old insulin-dependent diabetic man had a callus pared. Gangrene resulted, involving his left third, fourth and fifth toes and adjacent foot. One year previously, an ulcer of the same foot had healed with conservative treatment. Pedal pulses were absent but he did not have claudication or rest pain. On this admission, the pedal pulses were absent to palpation and the Doppler blood pressure in the posterior tibial artery was the same as the brachial pressure. The popliteal pulse was present and angiography showed a tight stenosis of the posterior tibial artery, which was the only one supplying the foot. Percutaneous transluminal angioplasty of the posterior tibial artery was done and a palpable pulse was restored at the ankle; a transmetatarsal amputation of the third, fourth and fifth toes healed with delayed skin grafting. He was fully weight bearing with a minimal limp postoperatively.

Four months after the initial amputation, rest pain, ulceration and breakdown of the skin grafts developed with necrosis of the second toe. The posterior tibial pulse was absent and angiography showed reocclusion of the posterior tibial artery. A popliteal posterior tibial saphenous vein graft was successful although the second toe had to be amputated. He was pain free and fully weight bearing with a patent saphenous vein graft 18 months after the initial amputation, when he died of esophageal varices.

Comment.—Adequate collateral circulation did not develop after the angioplasty and the patient lost another toe when the artery became occluded a second time. In the light of our present knowledge of angioplasty of the tibial arteries, bypass grafting should have been done initially rather than angioplasty.

Case 3

A 58-year-old man was seen in the emergency department with gangrene along the lateral edge of his right foot. The rest of the foot was swollen, painful and warm. Pedal pulses were absent but the popliteal pulse was present. Although diabetes mellitus had not been diagnosed previously, his blood glucose level was 21.1 mmol/L. He had no history of claudication or rest pain in his extremities.

Angiography showed diffuse disease in the proximal tibial and peroneal arteries with a patent distal posterior tibial artery supplying the foot. An autogenous reversed saphenous vein graft was inserted from the popliteal to the tibial arteries and the fifth toe and gangrenous tissue were amputated. Further débridement was done 1 week later. After 3 weeks of dressing changes to the open amputation site, the area was granulating, so skin grafting was done. At present, the saphenous vein graft has been patent for 1½ years and he is fully weight bearing with a healed amputation site.

Comment.—High skin temperature and erythema may not indicate adequate perfusion because a hyperdynamic circulation accompanies the inflammatory response to infection and gangrene. Revascularization should be done as early as possible after gangrene develops.

Case 4

A 48-year-old insulin-dependent diabetic man had gangrene of his left fifth toe and adjacent foot. The foot was edematous and warm without pedal pulses. No Doppler signal was audible in either pedal artery; the popliteal pulse was present. He had had no symptoms of vascular insufficiency in the past.

Angiograms showed disease of the peroneal and tibial vessels in the calf with the foot supplied by the terminal anterior tibial artery (Fig. 3).

Because his own saphenous vein was thrombosed, an umbilical vein graft was inserted from the popliteal to the anterior tibial artery and the fourth and fifth toes were amputated. Delayed skin grafting was done after the open

FIG. 1—Case 1. Large patent distal posterior tibial artery fed by collaterals. Peroneal and anterior tibial arteries cannot be seen.

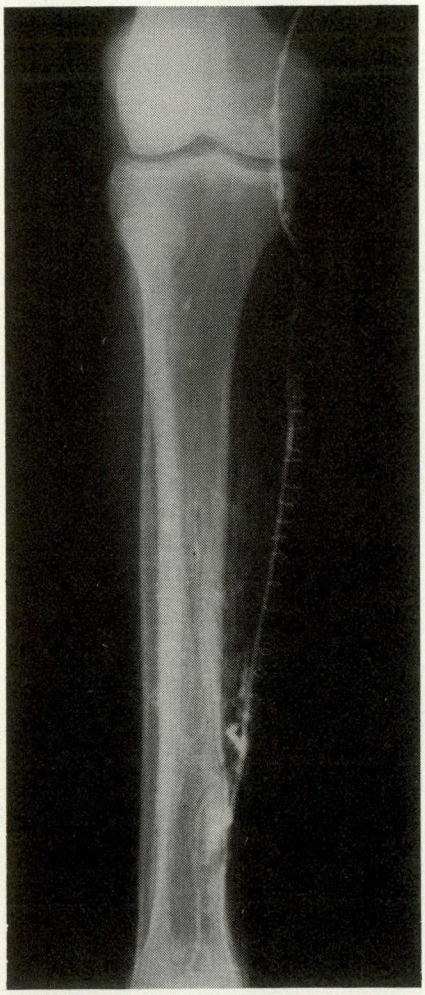

FIG. 2—Case 1. Operative arteriogram demonstrates saphenous vein graft filling posterior tibial artery.

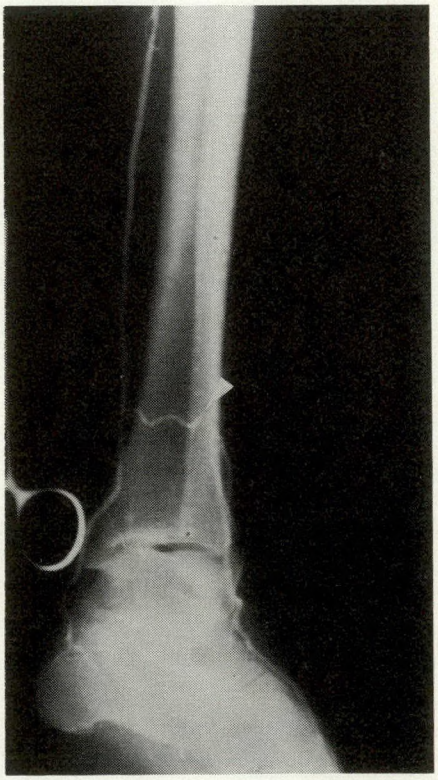

FIG. 3—Case 4. Patent posterior tibial artery that makes minimal contribution to blood supply of foot. Collateral with critical stenosis (arrow) supplies large patent distal anterior tibial artery, which is main vessel supplying foot.

amputation site granulated with dressing changes.

The umbilical vein graft became infected and occluded after 4 months but the skin grafts had healed by that time and the umbilical vein graft was removed without adverse effect.

He is fully ambulatory and pain free 2 years after the initial amputation.

Comment.—The umbilical vein graft provided temporary revascularization while the gangrene was treated, the skin grafts healed and collaterals developed. Salvage rates are usually higher than graft patency rates for this group of patients. In retrospect, the saphenous vein thrombosis may have been due to the gangrene and the vein from the other leg may have been suitable for grafting.

Case 5

Gangrene of the tip of the right middle toe developed in a 61-year-old grossly obese insulin-dependent diabetic woman. The foot was warm and painful with erythema of the toe and foot adjacent to the gangrene. No pedal pulse was palpable and a faint signal was heard by Doppler in the dorsalis pedis artery. The popliteal pulse was not palpable but the femoral pulse was present. She had no history of peripheral vascular insufficiency. The arteriogram showed a critical stenosis of the superficial femoral artery with some diffuse disease. The anterior tibial and peroneal arteries were thought by the radiologist to be occluded and there was no flow in the distal posterior tibial artery. Because of the lack of collaterals in the calf and the faint Doppler signal in the pedal arteries, the surgeon thought the problem was low flow rather than occlusion. A femoropopliteal umbilical vein graft was inserted because her own saphenous vein was thrombosed; good flow returned to both pedal arteries. The tip of her toe autoamputated and she is fully ambulatory and pain-free 1½ years postoperatively.

Comment.—Angiograms need to be interpreted in the light of the clinical findings and a positive Doppler signal may indicate a patent artery not visualized by angiography. An umbilical vein graft can be used as an arterial substitute when the patient's saphenous vein is not suitable.

Case 6

A 68-year-old man with insulin-dependent diabetes mellitus had painful gangrene of the pulps of the left ring and fifth fingers. The pulses of the left upper extremity were absent and angiography showed occlusion of the left subclavian artery. An axilloaxillary saphenous vein graft revascularized the left upper extremity and the fingers have remained healed for 1 year. No amputation or skin grafting was required.

Comment.—Diabetic gangrene may involve the upper as well as the lower extremity.

Discussion

Diabetic patients with gangrene may be extremely ill initially due to infection adjacent to the gangrene and to uncontrolled diabetes mellitus. Preoperatively, fluid, electrolyte, acid-base and blood-glucose abnormalities are corrected and antibiotics (usually an aminoglycoside) are administered parenterally. The antibiotics can be changed postoperatively as the culture results indicate. Roentgenograms may show associated bone destruction or gas in the soft tissues adjacent to the gangrene. Drugs such as acetylsalicylic acid, dipyridamole[4] and ibuprofen[5] are more effective in prolonging vein graft patency if they are begun preoperatively, and there is evidence that vitamin A[6] and prostaglandins[7] are beneficial although they are seldom used. Cessation of smoking is imperative and lipid abnormalities and obesity can be dealt with postoperatively.

Vascular disease may occur in both insulin-dependent and noninsulin-dependent diabetic patients; the exact relation of the vascular lesions to the control of blood glucose remains debatable.[8] The large-vessel lesion in diabetes mellitus is similar pathologically to that seen in nondiabetic patients with atherosclerosis although the diabetic atherosclerotic lesions are more numerous and more often complicated by ulceration, calcification and superimposed thrombosis.[3] Peripheral occlusive vascular disease is primarily due to atherosclerosis and is not related to medial calcification, which is also common in diabetic patients.[1] The degree of narrowing of a vessel required to produce a detectable pressure gradient or reduction in blood flow is called the critical stenosis and this is present when the cross-sectional area of the lumen is reduced by 75% or the diameter by 50%.[9] The pressure drop across a stenosis varies with the flow which explains why unimportant stenoses at rest become important with the increased flow of exercise, and claudication pain results. The inflammatory response to an infected, gangrenous extremity is a hyperdynamic circulation and this increased flow makes a stenosis more important. Arterial obstructions will be partially compensated for by collaterals that increase as a result of the increased flow velocity through the normal collateral vessels or as a result of the abnormal pressure gradient across the collateral bed.[10] The collaterals may look impressive by arteriography but their resistance is always greater than that of an unobstructed vessel. If a collateral vessel is one-fourth the diameter of the main artery, 256 vessels are required to equal the resistance of the original artery.[9]

The blood supply to a diabetic limb with gangrene is difficult to assess clinically, especially when active infection is also present and the inflammatory response to infection increases the skin temperature, causing erythema and edema that make pulses difficult to feel. The circulation may be hyperdynamic and cause arterial stenoses to become more important. Doppler studies and pedal artery blood pressures are useful and a positive Doppler signal may indicate a patent artery not visualized by angiography.[11] The clinical assessment is probably the best method of determining the need for revascularization; the surgeon should take into consideration skin temperature, rest pain, rubor, trophic changes and palpability of pulses. Any diabetic patient with gangrene and absent pulses should be considered for arteriography and possible vascular reconstruction. Occasionally, infection and edema adjacent to the gangrene will have spread to involve the operative site of revascularization and it is usually prudent to delay the revascularization in this situation because antibiotics, elevation of the extremity and excision of the gangrenous area will usually clear the infection and edema from the operative sites of revascularization. The angiographer should be informed that details of the distal arteries are required and that a hyperdynamic circulation may alter the film sequence. He should also look for proximal disease which may be occult.[12]

Although angiographic techniques can frequently be used as an aid or alternative to surgery,[13] Johnston and associates[14] have reported that percutaneous transluminal angioplasty of the tibial arteries is associated with a high incidence of occlusion. However, angioplasty may be useful for patients who are not candidates for major reconstructive surgery, as a temporizing measure while they are being prepared medically preoperatively, or for proximal lesions in larger arteries. Hess and associates[15] have reported arterial patency at 2 weeks in only 70 of 136 patients after the use of intra-arterial streptokinase and transluminal angioplasty.

The basic surgical principle in treating gangrene is to remove the dead tissue and to preserve the remaining healthy tissue by preventing the spread of infection and necrosis. If the remaining tissue is ischemic, antibiotics will not prevent the spread of infection and gangrene and revascularization will be necessary. The revascularization procedure may challenge the ingenuity of the surgeon; he may have to insert an extra-anatomic bypass graft or a graft to a small artery such as the tibial, peroneal or pedal.[16-20] Autogenous saphenous vein is the preferred material for grafting and sequential grafts can be used from the femoral to the popliteal and then to the tibial arteries if the superficial femoral and tibial arteries are both involved. Because gangrene of a foot can cause thrombosis of the autogenous saphenous vein, a preoperative venogram of the uninvolved leg should be considered to assess saphenous

vein patency because the vein from the unaffected leg may be required. Verta[21] has reported excellent results, grafting into arteries of the foot using saphenous vein and composite saphenous vein-polytetrafluoroethylene (PTFE) as sequential and nonsequential grafts. Polytetrafluoroethylene used as a noncomposite graft was not as successful. Reichle and associates[22-24] established the value of grafts from the common femoral artery to the tibial or peroneal arteries when the popliteal artery was occluded. Feldman and colleagues[25] have recently reported patency in 7 of 11 grafts to the distal tibial from the popliteal or proximal posterior tibial arteries. Umbilical vein grafts are superior to PTFE grafts and should be used when the autogenous vein is not available.[26,27] The Prolene mesh that now surrounds the umbilical vein grafts is designed to prevent aneurysm formation that was a complication of the unprotected grafts. Endarterectomy is not recommended below the knee although popliteal endarterectomy is feasible.[28] If more than one half of the sole of the foot has been destroyed, the limb will never be suitable for weight bearing despite effective arterial reconstruction. Amputation should be the initial treatment.[29] Revascularization occasionally will allow a below-knee amputation rather than an above-knee amputation. Failures of revascularization are usually due to an inadequate outflow and sympathectomy may be useful although diabetic patients often have reduced sympathetic activity. Ideally, revascularization should be done before any amputation because the earlier the blood supply can be restored to an extremity the less likelihood there is of further tissue loss.

Small areas of dry gangrene may be left to autoamputate if there is no associated pain or infection; usually, however, conservative amputation and débridement of obviously nonviable tissue is required. Unless the gangrene is dry with no associated infection, delayed closure of the wound is indicated and it may be several weeks before the site is suitable for closure. Even with revascularization and after several weeks of open treatment, the graft beds may not be ideal because of irregularities, the presence of fascia, bone, residual infection and microvascular diabetic changes. "Postage stamp" split-thickness skin grafts can be used to avoid common causes of graft failure; these are hematoma under the grafts, motion of the grafts and exudate from residual low-grade infection.

Conclusions

The extremities of diabetic patients are prone to peripheral vascular occlusive disease and any resulting ischemia potentiates infection and gangrene. Absent distal pulses in a diabetic extremity with gangrene should alert the clinician to the possibility of vascular reconstruction, which should be done as early as possible. The revascularization procedure, which may involve extra-anatomic or small-vessel grafting, will avoid a major amputation; it is surprising how much healing occurs when the blood supply has been restored.

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Bon Mots

Morals being what they are, it is not surprising that parts of the body that are well covered with skin, fat, hair and, formerly, by modesty, are now much more exposed — for example, the public tubercle.

Due to discoveries of a Canadian biochemist, Copp, we know now that the salmon is responsible for the production of a good amount of calcitonin. But what of the lowly herring? Is that species responsible for the production of heparing?

Pathologists, in particular, use foods to describe appearances of organs and tissues. The surgeons are following suit. That is why gastroplasty is sometimes followed by a dumpling syndrome.

Surgeons have described various types of rectal and anal repair in these pages as pre- and post-, but surely not postal!

I can understand the word psychiatric to describe a person, a therapy, a philosophy or a discipline but what kind of person is a psychiatrick?

The other hospitals should drool with envy when I hear patients express a preference for the Salivation Army Hospital.

JOSEPH L. SHUGAR, MD, FRCS[C]

Senior Associate Editor

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Acute Dissection of the Descending Thoracic Aorta: Repair in an Unusual Case

Acute tamponade, although a rare manifestation of a descending thoracic aneurysm, was the dominant clinical feature of a classic type III dissecting aneurysm (arising distal to the left subclavian artery) in a 52-year-old man. High-quality aortography confirmed the diagnosis, ruling out any anomaly of the ascending aorta and the aortic arch. Surgical treatment was carried out 24 hours after the initial episode without cardiopulmonary bypass. Through a left thoracotomy, a Gott shunt was inserted proximally at the apex of the left ventricle and distally in the left femoral artery. Aortic repair with the interposition of a 30-mm woven Dacron prosthesis was successful. Postoperative aortography showed complete restoration of aortic integrity.

La tamponnade cardiaque est une manifestation plutôt inattendue d'une lésion aiguë au niveau de l'aorte thoracique descendante. Nous l'avons observée comme manifestation principale d'une dissection aiguë de type III. L'aortographie thoracique a confirmé le diagnostic tout en éliminant la moindre anomalie au niveau de l'aorte ascendante et de la crosse aortique. La réparation chirurgicale a été réalisée par thoracotomie gauche avec la protection d'une dérivation externe (shunt de Gott) insérée proximalement dans la pointe du ventricule gauche et distalement dans l'artère fémorale gauche. Une interposition d'une prothèse de Dacron tissée de 30-mm a permis de rétablir l'intégrité aortique observable sur l'aortographie postopératoire.

Cardiac tamponade is a well-known complication of dissecting aneurysms originating in the ascending aorta (types I and II).[1] It is also a rare but usually fatal outcome of some dissecting aneurysms arising distal to the left subclavian artery (type III).[2] The mechanism, as observed at autopsy, is usually a retrograde dissection into the pericardium with or without a second rupture of the intrapericardial aorta. In our case, cardiac tamponade was the dominant clinical picture in a type III dissecting aneurysm without retrograde dissection.

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Case Report

A 52-year-old man with a history of untreated hypertension had sudden onset of chest pain followed rapidly by shock. The pain was localized to the interscapular area with radiation to the anterior middle part of the chest. The patient complained of transient weakness of the left lower limb. Signs of cardiac tamponade were obvious on examination. Blood pressure was 80/70 mm Hg and the central venous pressure was 26 cm H_2O. The electrocardiogram was normal, ruling out a cardiac infarction, and the chest roentgenogram showed superior mediastinal widening and a double aortic knob contour (Fig. 1), suggesting a lesion at this level.

At pericardiocentesis, 200 mL of nonclotting red blood were withdrawn. The patient immediately improved and allowed us time to transfer him safely to the angiography department.

Aortography demonstrated a classic type III dissecting aneurysm (Fig. 2). Aneurysmal dilatation was present distal to the left subclavian artery. The true lumen was irregular because of compression by the clotted false channel. The dissecting process extended to the diaphragm.

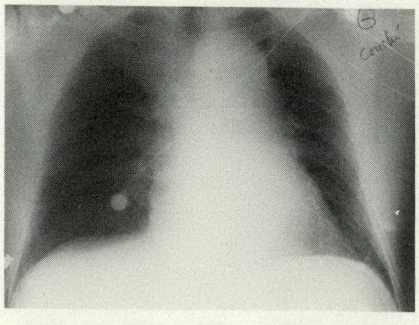

FIG. 1—Plain film shows widened mediastinum and double aortic shadow at level of aortic knob.

Soon after the dye injection, the cardiac tamponade recurred, complicated by a supraventricular tachycardia (160 beats/min). A blood pressure of 80/60 mm Hg was recorded through a right radial arterial line and the central venous pressure was 30 cm H_2O. Pericardiocentesis allowed aspiration of 300 mL of red blood and resulted in better and definitive heart decompression.

The blood pressure stabilized at 180/90 mm Hg and the central venous pressure at 15 cm H_2O. Full digitalization was initiated and metabolic acidosis corrected. Nipride solution was administered intravenously to lower the blood pressure to between 100 and 120 mm Hg systolic. The hyperkinetic heart was controlled with intravenous administration of propranolol.

The patient was operated on the following morning. Supraventricular tachycardia, which occurred upon induction of anesthesia, was easily controlled with an intravenous injection of propranolol.

Our standard procedure for lesions of the descending thoracic aorta was used.

Blood pressure and gas levels were recorded continuously through a right radial arterial line. A standard endotracheal tube is preferred for full inflation of both lungs and maximum oxygenation during the period of aortic cross clamping. Autotransfusion is used. For minor losses from the intercostal arteries, the blood is saved in a reservoir primed with

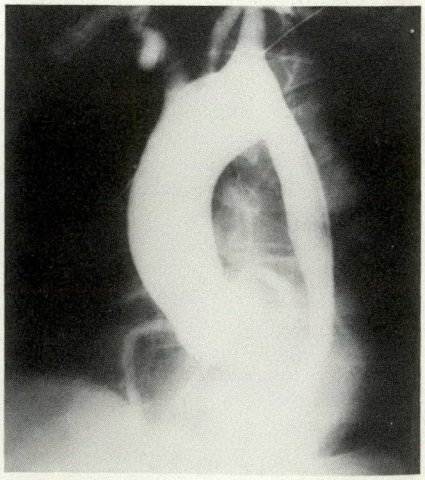

FIG. 2—Type III dissecting aneurysm. Preoperative aortogram showing irregular true lumen compresssed by clotted false channel. Ascending aorta is normal. Pathologic process starts distal to left subclavian artery.

diluted heparin and is retransfused when normal aortic circulation is restored. During the period of aortic cross-clamping, the aortic flow is diverted through a Gott heparin-coated shunt (Sherwood Medical Industries, St. Louis, Mo.), placed between the ascending aorta proximally and the descending aorta or left femoral artery distally. No systemic heparinization is required. This method of aortic shunting provides excellent proximal decompression of the brain and the heart and optimal distal perfusion of all organs and of the spinal cord.

The lesion was approached through the bed of the resected fifth rib. There was 300 mL of free red blood in the left pleural cavity. All of the aortic arch and the descending thoracic aorta had a reddish appearance; the adventitial and pleural layers were under extreme tension.

The pericardium was opened anterior to the left phrenic nerve and 100 mL of old blood evacuated from the pericardial sac. No active bleeding was identified. The ascending aortic wall was normal to palpation but its surrounding adventitia was quite infiltrated in continuity with the mediastinal hematoma.

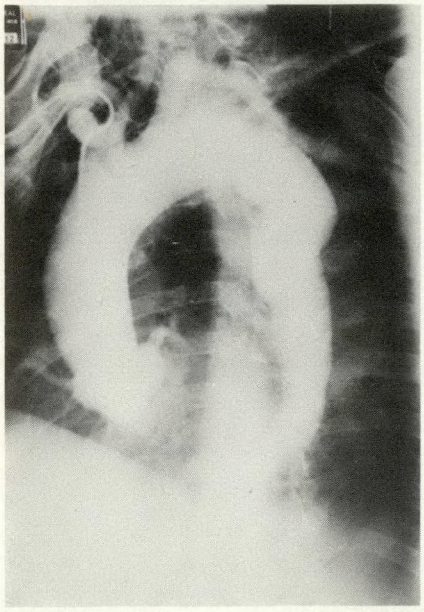

FIG. 3—Postoperative thoracic aortogram shows complete disappearance of false channel. True aortic lumen has more normal calibre.

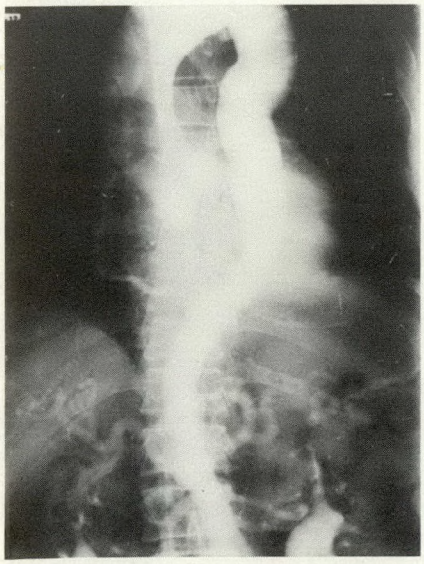

FIG. 4—Postoperative abdominal aortogram shows normal origin of major aortic branches from true aortic lumen.

Because of its suspected friability, the ascending aorta was thought unsuitable for proximal cannulation and the apex of the left ventricle was used instead. The distal part of the Gott shunt was introduced into a 10-mm, side-branch, woven Dacron prosthesis anastomosed end-to-side to the left femoral artery.

Vascular clamps were applied on the aortic arch between the left carotid and the left subclavian arteries, on the descending aorta and on the left subclavian artery. The descending aorta, where an obvious aneurysmal dilatation was noted, was incised distal to the left subclavian artery. The dissecting process involved two thirds of the aortic circumference and the false lumen was full of fresh clots. No intimal tear was seen. Eight centimetres of aneurysmal dilatation was resected. The dissected aorta was closed proximally and distally by incorporating a Teflon strip between the two separated medial layers. Then, a 30-mm woven Dacron graft was sutured proximally and 8 cm distally to re-establish aortic continuity. The postoperative course was smooth and the patient was soon started on long-term antihypertensive drugs.

On the 10th postoperative day, controlled aortography was performed. The ascending aorta and aortic arch appeared normal in size and configuration (Fig. 3). The woven graft with proximal and distal anastomoses was well visualized and appeared normal. The descending thoracic aorta had assumed a more normal calibre, although it was slightly irregular. All the major abdominal arteries were perfused normally through the true aortic channel (Fig. 4).

Discussion

The source of the cardiac tamponade was of concern in this case when emergency aortography showed a type III dissecting aneurysm. Despite high-quality angiography, no secondary intimal rupture could be identified in the intrapericardial aorta. The patient would not have survived an intrapericardial hemorrhage coming from a retrograde dissection and a secondary intimal rupture in the ascending aorta. Based on this clinical assertion, surgical repair was planned as for a standard type III dissecting aneurysm.

The cardiac tamponade was explained on the basis of extensive subadventitial dissection from the initial aortic wall rupture in the descending aorta. Blood under pressure had separated the adventitial and pleural layers towards the pericardial reflection. Diffusion of blood under pressure through the pericardium is possible; this process may cause a hemothorax when blood diffuses through the pleura. A right hemothorax has been reported in type III dissecting aneurysm.[3] This mechanism can also explain the hemopericardium found in a few cases of traumatic rupture of the descending thoracic aorta without underlying cardiac injury.[4] We recently treated a patient with a classic traumatic isthmic rupture of the descending thoracic aorta whose main clinical feature was cardiac tamponade.

Conclusions

Median sternotomy would have been disastrous in our patient if it had been taken for granted that the cardiac tamponade was coming from dissection of the ascending aorta. This case emphasizes the need for complete, high-quality aortography in all cases involving the thoracic aorta before an emergency surgical procedure is performed.

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3. FARACI PA, PAYNE DD, CLEVELAND RJ: Type III aortic dissection with rupture into the right hemithorax. *J Cardiovasc Surg (Torino)* 1982; 23: 429–31
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NOTICES

Call for Abstracts: Stereotactic and Functional Neurosurgery

The 9th meeting of the World Society for Stereotactic and Functional Neurosurgery will be held July 4–7, 1985 at the Chelsea Hotel and the University of Toronto, Toronto, Ont. It will be immediately followed by the International Congress of Neurological Surgery.

Abstracts must be of original work, not previously presented or published or accepted for publication, and they should be no longer than 250 words. The deadline for submission of abstracts is Sept. 1, 1984. Proceedings of both meetings will be published in *Applied Neurophysiology.*

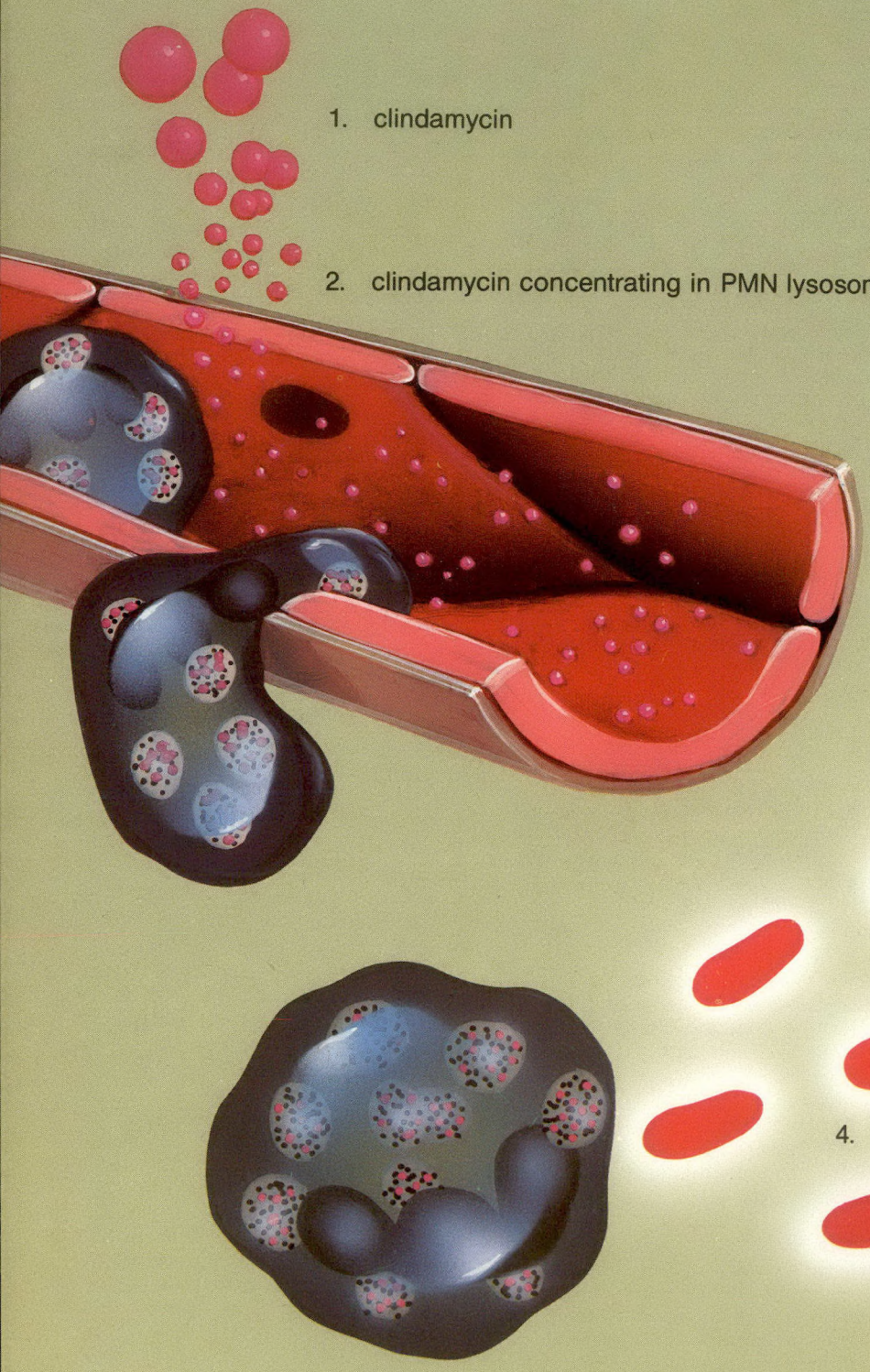
In order that presentations may be coordinated between the two meetings, all abstracts should be sent to: Dr. R.R. Tasker, Eaton Bldg. North 7-221, Toronto General Hospital, 101 College St., Toronto, Ont. M5G 1L7. For further information please write Mrs. Rae Ryan, Administrative Coordinator, Division of Neurosurgery, Eaton Bldg. North 7-221, Toronto General Hospital, 101 College St., Toronto, Ont. M5G 1L7 or call (416) 595-3443.

continued on page 407

Recent Research Suggests...

DALA

(clindamycin phosphate)



1. clindamycin

2. clindamycin concentrating in PMN lysosomes

3. clindamycin-laden PMN moving toward the site of infection

4. the invading bacteria

CIN® C Phosphate S.S.

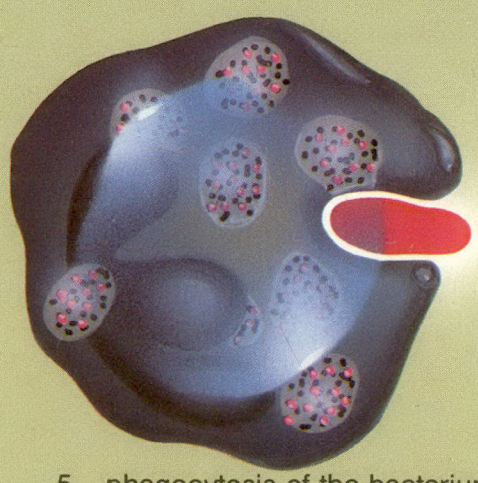
enhances

HOST DEFENSE

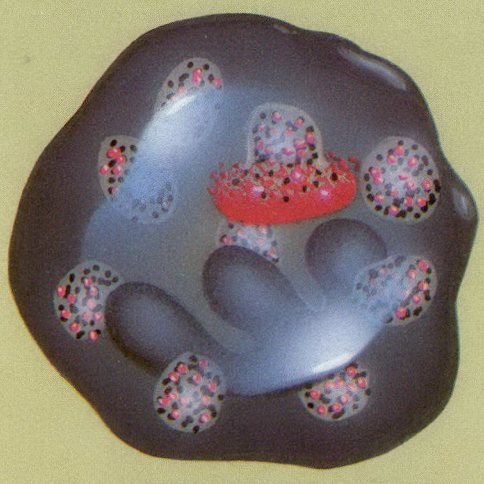
Recent *in-vitro* research has shown that clindamycin concentrates within the PMN in amounts greater than are found outside of the PMN.[1] The rates of chemotaxis, phagocytosis and killing of bacteria by PMNs are also enhanced by the presence of this antibiotic.[2,3] These characteristics may help explain clindamycin's outstanding record of clinical efficacy in both anaerobic and gram-positive aerobic infections.

Since host defense factors may be crucial in determining the outcome of an infection, selection of antibiotics based on host defense parameters may become a trend in infectious disease therapy.

1) Klempner MS, et al (Nov 1981) J Infect Dis *144*(5)
2) Johnson JD, et al (March 1980) J Lab Clin Med *95*(3)
3) Gemmell C, et al (1980) Current Chemotherapy and Infectious Disease (eds. J Nelson, C Grassi) Am Soc Microbiol Vol 2



5. phagocytosis of the bacterium by antibiotic-enhanced PMN



6. degranulation and killing of engulfed bacterium

Dalacin® C Phosphate Phosphate S.S.

Recommended Applications

Action: Clindamycin exerts its antibacterial effect by causing cessation of protein synthesis and also by causing a reduction in the rate of synthesis of nucleic acids.

Indications: Dalacin C Phosphate (clindamycin phosphate) is indicated for the treatment of infections where the oral route is not indicated or feasible.

Dalacin C Phosphate is indicated in the treatment of serious infections due to sensitive anaerobic bacteria, such as Bacteroides species, peptostreptococcus, anaerobic streptococci, Clostridium species and microaerophilic streptococci.

Dalacin C Phosphate is also indicated in serious infections due to sensitive Gram-positive organisms (staphylococci, including penicillinase-producing staphylococci, streptococci and pneumococci) when the patient is intolerant of, or the organism resistant to other appropriate antibiotics.

Contraindications: The use of Dalacin C Phosphate (clindamycin phosphate) is contraindicated in patients previously found to be hypersensitive to this compound, the parent compound, clindamycin, or clindamycin palmitate. Although cross-sensitization with Lincocin® (lincomycin hydrochloride) has not been demonstrated, it is recommended that Dalacin C Phosphate not be used in patients who have demonstrated lincomycin sensitivity.

Until further clinical experience is obtained, Dalacin C Phosphate is not indicated in the newborn (infants below 30 days of age), or in pregnant women.

Warnings: Some cases of severe and persistent diarrhea have been reported during or after therapy with Dalacin C Phosphate (clindamycin phosphate). This diarrhea has been occasionally associated with blood and mucus in the stools and has at times resulted in acute colitis. When endoscopy has been performed, some of these cases have shown pseudomembrane formation.

If significant diarrhea occurs during therapy, this drug should be discontinued or, if necessary, continued only with close observation. Significant diarrhea occurring up to several weeks post-therapy should be managed as if antibiotic-associated.

If colitis is suspected, endoscopy is recommended. Mild cases showing minimal mucosal changes may respond to simple drug discontinuance. Moderate to severe cases, including those showing ulceration or pseudomembrane formation, should be managed with fluid, electrolyte, and protein supplementation as indicated. Corticoid retention enemas and systemic corticoids may be of help in persistent cases. Anticholinergics and antiperistaltic agents may worsen the condition. Other causes of colitis should be considered.

Studies indicate a toxin(s) produced by Clostridia (especially Clostridium difficile) may be a principal cause of clindamycin and other antibiotic-associated colitis. These studies also indicate that this toxigenic Clostridium is usually sensitive *in-vitro* to vancomycin. When 125 mg to 500 mg of vancomycin were administered *orally* four times a day for 5 – 10 or more days, there was a rapid observed disappearance of the toxin from faecal samples and a coincidental recovery from the diarrhea.

It should be noted that serious relapses have occurred up to one month after apparently successful treatment. A relatively prolonged period of continuing observation is therefore recommended.

Precautions: Dalacin C Phosphate (clindamycin phosphate), like any drug, should be prescribed with caution in atopic individuals.

Dalacin C Phosphate must be diluted for intravenous administration. (See Dosage and Administration)

The use of antibiotics occasionally results in overgrowth of nonsusceptible organisms – particularly yeasts. Should superinfections occur, appropriate measures should be taken as dictated by the clinical situation.

As with all antibiotics, perform culture and sensitivity studies in conjunction with drug therapy.

Since abnormalities of liver function tests have been noted occasionally in animals and man, periodic liver function tests should be performed during prolonged therapy. Blood counts should also be monitored during extended therapy.

Dalacin C Phosphate may be used in anuretic patients. Since the serum half-life of clindamycin in patients with impaired hepatic function is greater than that found in normal patients, the dose of Dalacin C Phosphate should be appropriately decreased. Hemodialysis and peritoneal dialysis are not effective means of removing the compound from the blood. Periodic serum levels should be determined in patients with severe hepatic and renal insufficiency.

Adverse Reactions: *Local.*

(a) *Intramuscular Injections:* Of 404 patients treated with Dalacin C Phosphate (clindamycin phosphate) intramuscularly (with a solution containing 150 mg/mL), six (1.5%) demonstrated local reactions as follows: Two complained of pain at the injection site, two demonstrated induration at the injection site and two developed sterile abscesses.

(b) *Intravenous Infusions:* Of 192 patients treated with Dalacin C Phosphate by intravenous infusion, 14 (7.3%) demonstrated local reactions. Eleven patients developed superficial thrombophlebitis and one patient developed both superficial and deep thrombophlebitis. The majority of these cases developed in conjunction with the use of indwelling I.V. catheters and it is difficult to know how much the drug contributed to the irritation. Two patients developed localized erythema, swelling and pain at the site of the infusion.

Systemic Side Effects: Twenty-eight patients of 596 treated with Dalacin C Phosphate (clindamycin phosphate) by either the intramuscular or intravenous routes developed systemic side effects as follows:

	Number of Patients
Rash	7
Urticaria	1
Pruritus	1
Fever, Leucocytosis	1
Nausea, with or without vomiting	1
Diarrhea (See also under "Warnings")	4
Hypotension	1
Hypertension	1
Shortness of Breath	1
Superinfection*	4
Cardiac arrest**	1
Bad or bitter taste in mouth	5

*Superinfection is a complication of antibiotic therapy in general and is not necessarily a true side effect of clindamycin phosphate.

**Due to underlying myocarditis in this patient.

Clinical and Laboratory Findings: Patients treated during clinical trials of Dalacin C Phosphate (clindamycin phosphate) were followed with clinical laboratory tests, including complete hematology, urinalysis and liver and kidney function tests. Some of these tests were abnormal initially and returned to normal during therapy with Dalacin C Phosphate, while others were normal initially and became abnormal during therapy. Overall evaluation of clinical laboratory values in these patients does not indicate that Dalacin C Phosphate therapy has a toxic effect on the hematopoietic, hepatic or renal systems. Transient elevations of serum transaminases have occurred in some patients, but other liver function tests (alkaline phosphatase, serum bilirubin) have not shown any tendency to increase and there have not been clinical signs of drug-induced hepatic toxicity.

Symptoms and Treatment of Overdosage: No cases of overdosage have been reported. No specific antidote is known. Doses as high as 1200 mg every six hours (4800 mg/day) by infusion for five days have been given without adverse effects.

DOSAGE AND ADMINISTRATION

Adults

Intramuscular Injection: 600 mg/day in 2 equal doses.

Moderately severe infections: 600 to 1200 mg/day in 2 or 3 equal doses.

Severe infections: 1200 to 2400 mg/day in 2, 3 or 4 equal doses. Intramuscular injections of more than 600 mg into a single site are not recommended.

Intravenous Administration: Dalacin C Phosphate (clindamycin phosphate) must be diluted prior to I.V. administration to a dilution of 300 mg in 50 ml of diluent (6 mg/ml) or more, and infused in not less than 10 minutes. Administration of more than 1200 mg in a single 1 hour infusion is not recommended. Dalacin C Phosphate should not be injected intravenously undiluted as a bolus.

Moderately severe infections: 900 to 1800 mg/day by continuous drip or in 2 or 3 equal doses, each infused over 20 minutes or longer.

Severe infections: 1800 to 2700 mg/day by continuous drip or in 3 or 4 equal doses, each infused over 20 minutes or longer. In life-threatening infections, doses of 2700 to 4800 mg/day by continuous drip or in 3 or 4 equal doses each infused over 20 minutes or longer may be given.

Dilution and infusion rates:

Dose	*Diluent*	*Time*
300 mg	50 ml	10 min.
600 mg	100 ml	20 min.
900 mg	150 ml	30 min.
1200 mg	200 ml	45 min.

Alternatively, drug may be administered in the form of a single rapid infusion of the first dose followed by continuous I.V. infusion as follows:

To maintain serum clindamycin levels	*Rapid infusion rate*	*Maintenance infusion rate*
Above 4 mcg/ml	10 mg/min. for 30 min.	0.75 mg/min.
Above 5 mcg/ml	15 mg/min. for 30 min.	1.00 mg/min.
Above 6 mcg/ml	20 mg/min. for 30 min.	1.25 mg/min.

Children: (Over one month of age)

Intramuscular injection: 10 to 15 mg/kg/day in 2, 3 or 4 equal doses.

Moderately severe infections: 15 to 20 mg/kg/day in 3 or 4 equal doses.

Severe infections: 20 to 30 mg/kg/day in 3 or 4 equal doses.

Intravenous Administration:

Moderately severe infections: 15 to 25 mg/kg/day by continuous drip or in 3 or 4 equal doses, each infused over 20 minutes or longer. In severe infections, it is recommended that children be given no less than 300 mg/day regardless of body weight. (Dilute Dalacin C Phosphate Sterile Solution in the same manner as for adults.)

Dilution and Compatibility:

4 ml (600 mg) Dalacin C Phosphate when diluted with 1000 ml of the following commonly used infusion solutions was found to be physically compatible and demonstrated no significant change in pH or antimicrobial potency over a period of 24 hours:

Sodium chloride injection
Dextrose 5% in water
Dextrose 5% in saline
Dextrose 5% in Ringer's Solution
Dextrose 5% in half-strength saline plus 40 mEq potassium chloride
Dextrose 2½% in Lactated Ringer's Solution (Hartmann's Solution).

Dalacin C Phosphate was not stable when added to Dextrose 5% in water plus vitamins. Therefore it is not recommended that Dalacin C Phosphate be mixed with any infusion solution containing B vitamins.

Supplied:

Dalacin C Phosphate contains the following per ml of sterile solution:

Clindamycin phosphate equivalent to clindamycin base 150 mg
Benzyl alcohol 5 mg
Disodium edetate 0.5 mg
Water for injection q.s.

When necessary the pH is adjusted with sodium hydroxide and/or hydrochloric acid to maintain a pH range of 5.5 to 7.0.

Dalacin C Phosphate is available in 2 ml and 4 ml ampoules.

NOTE: Do not store below 15°C.

Product Monograph available upon request. CE 1377.1C

THE UPJOHN COMPANY OF CANADA/865 YORK MILLS ROAD/DON MILLS, ONTARIO

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Right Ventricular Size and Ventricular Septal Motion after Repair of Atrial Septal Defect in Children

An enlarged right ventricle and abnormal ventricular septal motion are characteristic echocardiographic features of atrial septal defect and often persist after the defect has been completely closed, even when the operation clinically is judged to be successful.

These features were examined retrospectively 15 to 21 months after operation in a group of children whose atrial septal defect had been closed between January 1976 and July 1979. Despite satisfactory postoperative results in all, about two thirds had an enlarged right ventricular dimension and about the same number had abnormal septal motion when examined echocardiographically an average of 18 months after operation. The best operative strategy seems to be to operate while the right ventricular end-diastolic dimension is still relatively small in echocardiographic terms.

L'augmentation des dimensions ventriculaires droites et un mouvement septal anormal composent les éléments échocardiographiques qui caractérisent la communication interauriculaire. Cependant ces signes persistent après fermeture chirurgicale complète, et ce malgré un résultat clinique satisfaisant.

Une revue des études échocardiographiques fut conduite chez des enfants dont la communication interauriculaire fut réparée entre janvier 1976 et juillet 1979. Les deux tiers des patients présentent toujours une augmentation des dimensions ventriculaires droites en moyenne 18 mois après chirurgie. Un nombre à peu près identique présente un mouvement septal anormal. Ainsi, l'intervention devrait être planifiée plus tôt, alors que les dimensions ventriculaires droites sont dans les limites normales, à l'échocardiographie.

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Increased right ventricular end-diastolic dimension (RVED) and abnormal ventricular septal motion are the characteristic echocardiographic features of atrial septal defect; they often persist even after clinically successful complete closure of the defect.[1-4]

Postoperative data on right ventricular performance have been reported recently for 51 children by Meyer and associates[5] derived from serial echocardiograms taken 3 months to 5 years after closure of an atrial septal defect. The mean RVED of the group decreased maximally by 3 months with no further decreases up to 5 years; the mean RVED was always higher than that for 101 normal children of comparable age and size. Septal motion was normal in 55% by 3 months after operation and in 89% of those examined at 5 years. The investigators suggested that the persistent enlargement of the right ventricle was due to chronic overload and that surgical closure in the first 3 years of life might prevent it.

This study complemented the serial echocardiographic study of Meyer and associates. Our focus was on pre- and postoperative echocardiographic findings in individual children, related to the normal range, and whether any preoperative factors suggest a better operative strategy.

Patients and Methods

This study used echocardiographic measurements in children whose secundum atrial septal defect was repaired between Jan. 1, 1976 and June 30, 1979 in our hospital.

All echocardiographic tracings for these patients were reviewed. Only those for which a right ventricular cavity and septum could be identified were retained. Two copies were made of that portion, taken at or just below the level of the mitral valve tip.

Both copies of each tracing and a separate note identifying the child and date of the echocardiogram were assigned a unique code number from a random number table. This code number was the sole identifier on the tracings, which were arranged in numerical order and furnished to two readers (S.N. and H.F.). The code was not broken until after all tracings had been read, when clinical, cardiac catheterization and operative data that had been abstracted separately were merged with echocardiographic data.

The two readers measured RVED and classified septal motion as normal, flat or reversed, or noted that one or both were unmeasurable. Readings were reported separately by each reader to the data monitor (D.C.). If there was disagreement over whether a tracing could be read, if individual RVED measurements varied more than 10% from the mean of the two measurements or if judgement about the type of septal motion varied, the tracing was submitted to the head of our echocardiography service (W.J.D.) for arbitration.

We located 119 echocardiographic tracings. Several otherwise acceptable tracings were rejected when matched to clinical data — two because the children had Down's syndrome, one because the child had dextrocardia and one because the echocardiogram was taken immediately after operation for problems in the intensive care unit rather than as a normal follow-up procedure. The final yield for study was 98 tracings in which both RVED and septal motion could be read: 24 preoperative tracings (group 1), 18 postoperative tracings (group 2) and 28 pairs of pre- and postoperative tracings (group 3).

Echocardiographic Features

The right ventricular end-diastolic dimension was measured from the endocardium of the anterior wall of the right ventricle to the right side of the septum, at the level of the mitral valve, at the beginning of the QRS complex. Three complexes were measured on the majori-

ty of tracings (93.9%), at the expiratory phase which appeared to have the least respiratory variation, and the average of these measurements was taken for each child.

In 44 of the 52 patients (84.6%) in groups 1 and 3, the preoperative echocardiograms were obtained within 1 week of cardiac catheterization and in the remaining 8 patients (15.4%) from 2 to 46 months (mean 19.9 months) before the catheterization.

Protocols in the Division of Cardiology call for an echocardiogram 18 months after repair of an atrial septal defect. Examinations in groups 2 and 3 took place from 0.2 to 51.1 months after operation (mean 20.5 months).

The normal range for RVED was defined according to the criteria of Gutgesell and Paquet,[6] which relate RVED to the cube root of weight.

Hemodynamic Features

All patients underwent right heart catheterization before operation (Tables I to III). Left-to-right shunt size was determined by the Fick principle and expressed as the pulmonary to systemic flow ratio (Qp:Qs). Right ventricular and pulmonary artery pressures were recorded in every case.

Intraoperative Measurements

The major and minor diameters of the defect were measured during operation for every child. Estimates were made of the defect area by assuming that all defects were elliptical.

Statistical Methods

Simple and multiple regression analyses were carried out to seek the best explanatory variables for RVED and septal motion. This involved a step-up procedure to select the data that correlated most strongly with RVED or septal motion, or both. The relation of the change in RVED after operation to shunt size and right ventricular pressure at catheterization, age of the child and size of defect at operation and length of follow-up was examined by linear regression to determine whether a particularly favourable operative strategy could be derived. $P < 0.05$ was considered significant.

Results (Tables I to III)

Preoperative (Tables I and III)

In all 52 children (groups 1 and 3) the RVED was enlarged above the normal 99th percentile.[6] All but nine had abnormal septal motion; in about half of them, the septal motion was classified as reversed.

The right ventricular end-diastolic dimension correlated significantly ($p < 0.05$) with the child's age, with body surface area and with a score for type of septal motion, but not with any of the measurements obtained at cardiac catheterization. The septal motion score (1 = normal, 2 = flat, 3 = reversed motion) correlated significantly only with the RVED and the shunt at catheterization. There was no evidence that the type of septal motion, shunt size or pressures changed as the children aged; no child

Table I—Group 1. Results

Patient no.	Preop echocardiographic findings: Age, mo	RVED, mm	SM, type	Catheterization: Age, mo	Shunt, ratio	RVP, mm Hg	Age at operation, mo
1	4.0	18	R	4.1	3.4	32	4.3
2	22.9	20	F	23.0	4.0	54	25.6
3	37.6	26	R	37.5	3.7	42	37.6
4	39.6	20	N	39.6	2.4	40	42.0
5	43.6	25	R	46.3	3.4	24	46.4
6	44.8	20	N	56.8	2.3	41	90.0
7	48.3	21	F	60.3	1.8	29	65.1
8	52.5	24	F	52.2	3.7	30	54.4
9	53.3	19	F	7.3	2.5	36	56.9
10	53.9	23	N	53.9	2.8	24	57.4
11	57.2	24	R	57.2	2.2	33	57.3
12	61.6	28	N	61.6	2.9	26	61.7
13	61.9	23	F	61.9	2.1	32	62.0
14	62.0	24	R	62.0	2.7	44	62.1
15	70.8	21	N	70.8	1.8	33	73.3
16	74.7	32	R	74.8	2.2	35	76.6
17	75.8	23	F	31.3	2.1	25	78.7
18	82.0	26	R	82.0	4.0	61	82.0
19	89.1	20	F	89.3	1.6	30	90.7
20	108.6	37	R	104.4	4.0	33	108.7
21	111.1	33	R	111.1	5.0	37	111.2
22	146.1	32	F	146.2	2.0	35	162.8
23	148.2	29	N	148.2	2.4	28	148.3
24	176.9	34	F	176.9	2.4	29	177.0

RVED = right ventricular end-diastolic dimension, SM = septal motion, RVP = right ventricular pressure, N = normal, R = reversed, F = flat.

Table II—Group 2. Results

Patient no.	Catheterization: Age, mo	Shunt, ratio	RVP, mm Hg	Age at operation, mo	Postop echocardiographic findings: Age, mo	RVD, mm	SM, type
25	27.3	2.0	51	29.3	50.6	24	F
26	37.1	2.7	31	37.2	56.3	18	N
27	13.2	3.0	30	56.2	56.5	21	F
					81.6	23	N
28	30.1	2.3	40	47.9	65.3	22	N
29	54.1	3.1	56	54.1	74.4	23	F
30	8.5	2.5	36	50.2	81.1	16	F
31	57.7	3.0	58	60.7	81.7	12	F
32	11.8	2.1	24	50.1	85.1	14	N
33	52.5	2.3	35	54.3	85.4	18	F
34	68.6	4.2	50	68.7	85.5	18	N
35	72.6	2.2	40	73.4	91.3	23	F
36	72.3	1.9	41	80.1	96.9	21	N
37	66.1	3.0	35	70.2	100.8	19	N
38	46.3	1.8	30	94.0	110.0	19	F
39	98.5	3.1	20	100.5	139.6	13	N
40	111.9	2.6	36	112.0	152.7	27	F
41	168.3	1.9	45	173.0	192.1	29	F
42	192.6	2.1	25	201.2	219.4	22	F

RVED = right ventricular end-diastolic dimension, SM = septal motion, RVP = right ventricular pressure, N = normal, R = reversed, F = flat.

had more than one preoperative catheterization.

Postoperative (Tables II and III)

In approximately one third of the 46 children (groups 2 and 3) who had postoperative echocardiograms, the RVED was in the normal range. The same proportion had normal septal motion; no child had reversed motion postoperatively

Pre- and Postoperative (Table III)

In the 28 group 3 children who had echocardiograms both before and after operation, the RVED fell after operation in 25, remained the same in 1 but rose in 2. Before operation, all had RVED outside the 99th percentile of the Gutgesell and Paquet[6] norms; after operation, 10 fell within the normal range at the first postoperative echocardiographic examination and 2 more fell within the normal range at a later examination. Septal motion was normal in 9 (8 had abnormal motion preoperatively), remained flat in 6 patients and turned flat from reversed motion in 12, but also turned flat in 2 whose septal motion was normal preoperatively (Fig. 1).

The greatest fall in RVED was in those whose RVED had been largest before operation. However, because it was so markedly increased in these children, it was the patients with relatively minor preoperative increases in RVED who were most likely to be in the normal range after operation. There was little relation statistically between the time that had passed since operation and any decline in RVED (i.e., there was no evidence that a longer follow-up would produce more cases of normal RVED).

There were no significant differences in clinical factors between patients whose cardiac status returned to normal postoperatively and those whose status did not, other than the fact that grade 2 murmurs were still heard (in 3 of 16 patients) only among those with an abnormal RVED.

Regression analysis of the data on change in RVED did not pinpoint any preoperative strategy other than to operate on children while the RVED is still relatively small.

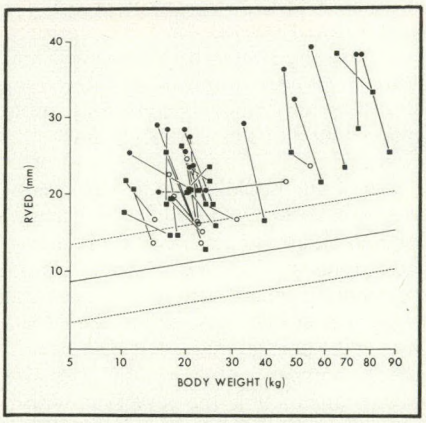

FIG. 1—Preoperative and postoperative right ventricular end-diastolic dimension (RVED) and septal motion (normal = white circles, flat = squares, reversed = black circles) related to body weight (shown on cube root scale) in 28 patients. Solid line = mean normal RVED, upper dotted line = 97.5th percentile, lower = 25th percentile.

Discussion

Right ventricular end-diastolic dimension is usually measured from the endocardium of the anterior wall of the right ventricle to the right side of the septum,[3,6,7] but the right ventricular wall can be poorly resolved on echocardio-

Table III—Group 3. Results

Patient no.	Preop echocardiographic findings: Age, mo	RVED, mm	SM, type	Catheterization: Age, mo	Shunt, ratio	RVP, mm Hg	Age at operation, mo	Postop echocardiographic findings: Age, mo	RVED, mm	SM, type
43	33.0	18	F	33.0	3.8	30	51.6	69.0	15	F
44	43.2	23	N	43.1	2.0	30	48.5	48.8	20	N
								73.2	16	N
45	43.7	30	R	43.6	4.0	42	43.7	75.8	13	F
46	52.6	21	R	50.6	2.9	27	55.0	75.2	21	F
47	53.8	24	R	53.8	2.6	30	58.2	79.9	22	F
48	57.9	29	R	22.0	2.5	28	58.0	85.8	19	F
49	59.7	26	F	59.7	3.3	43	59.8	77.7	18	F
50	59.9	21	F	59.9	1.5	54	66.0	83.1	14	N
51	60.2	26	R	60.2	1.8	50	60.2	88.5	21	F
52	61.1	27	F	61.1	2.2	50	61.2	81.6	21	F
53	61.7	22	F	61.7	2.8	55	66.5	83.2	17	N
54	62.9	20	R	62.9	2.3	30	62.9	81.1	15	F
55	63.4	29	R	63.8	3.6	48	63.8	64.0	19	F
56	64.5	21	N	64.4	2.2	28	64.5	80.2	24	F
57	70.5	20	F	70.5	1.5	30	70.6	105.0	15	N
58	72.0	20	F	72.0	2.2	33	73.6	91.5	16	F
59	77.1	26	R	77.1	2.5	35	83.0	88.5	17	N
60	83.3	24	R	83.3	2.6	32	83.4	102.3	19	F
								131.8	17	N
61	83.8	21	R	83.8	2.4	36	85.7	136.8	22	N
62	88.5	25	N	88.5	1.8	23	102.7	102.9	16	F
63	124.0	30	R	124.0	3.0	26	126.3	146.2	17	F
64	127.5	28	R	127.6	2.3	38	131.7	149.8	14	N
65	165.4	33	R	165.4	3.4	33	166.7	191.2	22	F
66	168.6	40	R	169.3	2.4	35	171.7	193.3	24	F
67	175.8	37	R	175.9	4.2	32	175.9	176.2	28	F
								205.7	24	N
68	199.3	39	F	199.2	2.0	29	199.3	220.6	29	F
69	199.7	39	R	199.7	3.4	25	199.8	223.7	26	F
70	203.2	39	F	203.2	1.7	28	207.0	227.3	34	F

RVED = right ventricular end-diastolic dimension, SM = septal motion, RVP = right ventricular pressure, N = normal, R = reversed, F = flat.

graphy.[7] In our study, only those with a clearly delineated right ventricular wall and ventricular septum were included.

Meyer[8] provided normal RVED values for children arranged by age, weight and height. However, the resulting normal range is a series of flat steps with the same normal RVED over fairly broad age categories of several years. We preferred to adopt the standard of Gutgesell and Paquet,[6] whose graph of RVED versus the cube root of body weight for 85 normal children gives a straight-line relationship.

All of our 52 children who had preoperative echocardiograms (groups 1 and 3) had an abnormal RVED but 9 had normal septal motion. Also, two with normal motion preoperatively developed flat motion after operation (in one the RVED was in the normal range postoperatively). Thus, normal septal motion does not always mean that the RVED is within normal limits nor does flat septal motion postoperatively always accompany an increased RVED.

None of our postoperative echocardiograms showed reversed septal motion. In adults with an atrial septal defect, reversed motion postoperatively has been related to persistent right ventricular dilatation while reversion to normal motion was a feature of those with relatively mild dilatation.[9]

The results obtained on evaluating septal motion may be ambiguous. In particular, calling the septal motion "flat" may mean only that the motion is not clearly either normal or reversed. Our two readers did not agree about the type of septal motion in 28 (23.5%) tracings, which thus had to be submitted to arbitration: only 7 (5.9%) of the 119 tracings involved one reader who believed motion was normal while the other thought it reversed. Similar proportions are found in studies of the reliability of clinical methods and judgement.[10-12]

Our data on diminished postoperative RVED are broadly consistent with the findings of Meyer and associates.[5] Eighteen months after operation, two thirds of our patients had an RVED outside the normal range. Use of the mean RVED to measure group change (as in Meyer's study) could mask the benefits of operation in individual patients. We cannot explain the marked disparity in findings on septal motion (29% [8 of 28] of our patients reverted to normal motion against 55% to 89% of theirs), but it is not clear whether our patients and classification criteria were sufficiently similar to permit direct comparison. Finally, the conclusions of both groups about operative strategy have similar effects although grounded and phrased differently.

Our conclusions are based on single follow-up echocardiograms, which most patients had. (Four patients had a second tracing sometime after operation; RVED continued to decrease in three, and in two fell into the normal range on the later tracing.) Because our patients, by and large, were seen between 15 and 21 months after operation, the data are insufficient to plot immediate or long-term postoperative changes. Future studies should include serial echocardiograms, or at least cross-sectional studies should use different follow-up intervals from the one used in this study.

Most of our patients were operated upon between 3 and 6 years of age. So far, we have not repaired an atrial septal defect at an earlier age unless the pulmonary-to-systemic flow ratio was greater than 2.5:1. We found that the patients with less extreme preoperative increases in RVED were most likely to be in the normal range after operation. This suggests that operative repair might best be carried out while the RVED, as measured by echocardiography, is still close to normal.

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MANUEL MEDINA, MD; RAO R. IVATURY, MD, FRCS[C]; WILLIAM M. STAHL, MD, FACS

Omental Evisceration through an Abdominal Stab Wound: Is Exploratory Laparotomy Mandatory?

The authors reviewed and analysed the records of 75 patients with omental and bowel evisceration as a result of abdominal stab wounds to discover whether omental prolapse makes laparotomy mandatory. Major intra-abdominal injuries were found in 82.7% of the total group, 82.9% in those with omental protrusion and 82.5% in patients with bowel prolapse. The nature of the injuries and the incidence of multiple organ trauma were similar in the two groups. Negative laparotomy did not cause important morbidity. The authors conclude that omental herniation after stab wounds of the abdomen should routinely prompt exploratory celiotomy.

Les auteurs passent en revue et analysent les dossiers médicaux de 75 patients victimes d'une éviscération de l'intestin et de l'épiploon à la suite d'un coup de couteau à l'abdomen, dans le but de vérifier si un prolapsus de l'épiploon commande une laparotomie. Des blessures abdominales graves ont été constatées chez 82.7% du groupe, chez 82.9% du groupe ayant une protrusion de l'épiploon et chez 82.5% de ceux qui avaient un prolapsus intestinal. La nature des blessures et la fréquence des traumatismes à de multiples organes étaient semblables dans les deux groupes. Une laparotomie négative n'entraîne pas une morbidité importante. Les auteurs concluent qu'une hernie de l'épiploon devrait entraîner systématiquement une laparotomie exploratoire.

Selective exploration of patients with stab wounds of the abdomen, based on clinical observation,[1-3] local wound exploration, peritoneal lavage[4,5] or a combination of these methods,[6-8] has gained wide popularity. At our institution, while we have adopted the policy of "selective conservatism",[4] omental or bowel evisceration through stab wounds has been a mandatory indication for laparotomy. We have analysed our experience to determine whether such a practice is justified. We could find only one other series[9] in the English literature specifically addressing the issue of abdominal stab wounds with evisceration.

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Patients and Methods

We reviewed the records of all patients admitted to the Lincoln Medical and Mental Health Center between 1973 and 1983 with omental or bowel evisceration as a result of knife wounds to the abdomen. We did not include patients with multiple stab wounds in addition to the one with evisceration. We also excluded three patients with inadequate documentation and seven patients from earlier years of the study who were managed by amputation of the extruded omentum and clinical observation, because adequate follow-up could not be documented from their clinical records.

Seventy-five patients who satisfied the criteria for analysis constituted the study population. Seventy-two were men and 3 were women. The age range was 17 to 59 years. Five patients presented in shock (systolic blood pressure less than 70 mm Hg). The only other indication for laparotomy was evisceration of omentum (35 patients) and bowel (40 patients). All patients were resuscitated initially with Ringer's lactate and type-specific blood, if necessary, depending on hemodynamic status. Antibiotics (ampicillin, gentamicin and clindamycin) were administered preoperatively.

In the operating room the eviscerated bowel and omentum were copiously irrigated with normal saline and the bowel was replaced. The extruded omentum was amputated. The type of operative repair of the injured organs followed standard surgical principles. Small-bowel injuries were treated by repair or resection of involved bowel and anastomosis; colonic lacerations were managed by repair, colostomy or repair and exteriorization; pancreatic lesions were repaired with drainage; splenic wounds were treated by splenectomy or splenorrhaphy and bile-duct or vascular injuries were repaired. The stab-wound site was routinely closed by fascial sutures to prevent the subsequent development of traumatic hernia.

For the purpose of this study, laparotomy was considered positive only if major visceral damage was found; small mesenteric and retroperitoneal hematomas were not considered significant.

Results

Sixty-two of the 75 patients (82.7%) had serious intra-abdominal injury. The number of positive explorations was similar in the group with omental hernia-

Table I—Summary of Organ Injuries

Organ injured	No. with omental prolapse	No. with bowel prolapse
Colon	8	10
Small bowel	10	24
Stomach	3	4
Liver	7	5
Spleen	4	1
Pancreas	2	2
Kidney	0	1
Major blood vessels	6	5
Diaphragm	6	0
Extrahepatic bile ducts	2	0
	48	52

Mefoxin* IV/IM

ANTIBIOTIC

ACTION

In vitro studies demonstrate that the bactericidal action of cefoxitin, a cephamycin derived from cephamycin C, results from the inhibition of bacterial cell wall synthesis. Evidence suggests that the methoxy group in the 7α position is responsible for the resistance of cefoxitin to degradation by bacterial beta-lactamases.

INDICATIONS AND CLINICAL USES

TREATMENT

The treatment of the following infections when due to susceptible organisms:

1 - Intra-abdominal infections such as peritonitis and intra-abdominal abscess
2 - Gynecological infections such as endometritis and pelvic cellulitis
3 - Septicemia
4 - Urinary tract infections (including those caused by *Serratia marcescens* and *Serratia* spp.)
5 - Lower respiratory tract infections
6 - Bone and joint infections caused by *Staphylococcus aureus*
7 - Soft tissue infections such as cellulitis, abscesses and wound infections

Appropriate culture and susceptibility studies should be performed to determine the susceptibility of the causative organism(s) to MEFOXIN*. Therapy may be started while awaiting the results of these tests, however, modification of the treatment may be required once these results become available.

Organisms particularly appropriate for therapy with MEFOXIN* are:

Gram positive
Staphylococci, penicillinase producing and non-producing
Streptococci excluding enterococci

Gram negative (beta-lactamase producing and non-producing strains)
E. coli
Klebsiella species (including *K. pneumoniae*)
Proteus, indole positive and negative
Haemophilus influenzae
Providencia species

Anaerobes
Bacteroides fragilis

MEFOXIN* may also be appropriate for the treatment of infections involving susceptible strains of both aerobic and anaerobic bacteria.

Clinical experience has demonstrated that MEFOXIN* can be administered to patients who are also receiving carbenicillin, gentamicin, tobramycin, or amikacin (see PRECAUTIONS and ADMINISTRATION).

Intravenous Administration
The intravenous route is preferable for patients with bacteremia, bacterial septicemia, or other severe or life-threatening infections, or for patients who may be poor risks because of lowered resistance resulting from such debilitating conditions as malnutrition, trauma, surgery, diabetes, heart failure, or malignancy, particularly if shock is present or impending.

PROPHYLACTIC USE

MEFOXIN* may be administered perioperatively (preoperatively, intraoperatively and postoperatively) to patients undergoing vaginal or abdominal hysterectomy and abdominal surgery when there is a significant risk of postoperative infection or where the occurrence of postoperative infection is considered to be especially serious.

In patients undergoing cesarean section, intraoperative (after clamping the umbilical cord) and postoperative use of MEFOXIN* may reduce the incidence of surgery related postoperative infections.

Effective prophylactic use depends on the time of administration. MEFOXIN* usually should be given one-half to one hour before the operation. Prophylactic administration should usually be stopped within 12 hours. It has been generally reported that continuing administration of any antibiotic beyond 24 hours following surgery increases the possibility of adverse reactions but, in the majority of surgical procedures, does not reduce the incidence of subsequent infection.

If signs of postsurgical infection should appear, specimens for culture should be obtained for identification of the causative organism(s) so that appropriate therapy may be instituted.

*®Trademark

CONTRAINDICATIONS

MEFOXIN* is contraindicated in persons who have shown hypersensitivity to cefoxitin or to the cephalosporin group of antibiotics.

WARNINGS

Before therapy with MEFOXIN* is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to MEFOXIN*, cephalosporins, penicillins or other drugs. MEFOXIN* should be given with caution to penicillin-sensitive patients.

There is some clinical and laboratory evidence of partial cross-allergenicity between cephamycins and the other beta-lactam antibiotics, penicillins and cephalosporins. Severe reactions (including anaphylaxis) have been reported with most beta-lactam antibiotics.

Pseudomembranous colitis has been reported with virtually all antibiotics. This colitis can range from mild to life threatening in severity. Antibiotics should therefore be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis. It is important to consider a diagnosis of pseudomembranous colitis in patients who develop diarrhea in association with antibiotic use. While studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis, other causes should also be considered.

Any patient who has demonstrated some form of allergy, particularly to drugs, should receive antibiotics including MEFOXIN* with caution.

If an allergic reaction to MEFOXIN* occurs, administration of the drug should be discontinued. Serious hypersensitivity reactions may require treatment with epinephrine and other emergency measures.

PRECAUTIONS

The total daily dosage should be reduced when MEFOXIN* is administered to patients with transient or persistent reduction of urinary output due to renal insufficiency (see DOSAGE AND ADMINISTRATION) because high and prolonged serum antibiotic concentrations can occur from usual doses.

In patients treated with MEFOXIN* a false-positive reaction to glucose in the urine may occur with Benedict's or Fehling's solutions but not with the use of specific glucose oxidase methods.

Using the Jaffe Method, falsely high creatinine values in serum may occur if serum concentrations of cefoxitin exceed 100 μg/mL. Serum samples from patients treated with MEFOXIN* should not be analyzed for creatinine if withdrawn within two hours of drug administration.

Increased nephrotoxicity has been reported following concomitant administration of cephalosporins and aminoglycoside antibiotics.

The safety of MEFOXIN* in the treatment of infections during pregnancy has not been established. If the administration of MEFOXIN* to pregnant patients is considered necessary, its use requires that the anticipated benefits be weighed against possible hazards to the fetus. Reproductive and teratogenic studies have been performed in mice and rats and have revealed no evidence of impaired fertility or harm to the fetus due to MEFOXIN*.

Cefoxitin has been observed in the milk of nursing mothers receiving the drug.

Prolonged use of MEFOXIN* may result in the overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential and if super-infection occurs during therapy, appropriate measures should be taken. Should an organism become resistant during antibiotic therapy, another antibiotic should be substituted.

In children 3 months of age or older, higher doses of MEFOXIN* (100 mg/kg/day and above) have been associated with an increased incidence of eosinophilia and elevated SGOT.

The safety and efficacy of MEFOXIN* for the treatment of infections in infants from birth to three months of age have not yet been established.

ADVERSE REACTIONS

MEFOXIN* is generally well tolerated. Adverse reactions rarely required cessation of treatment and usually have been mild and transient.

Local Reactions
Thrombophlebitis has occurred with intravenous administration. Some degree of pain and tenderness is usually experienced after intramuscular injections using water. Induration has occasionally been reported.

Allergic
Maculopapular rash, urticaria, pruritus, eosinophilia, fever and other allergic reactions have been noted.

Gastrointestinal
Symptoms of pseudomembranous colitis can appear during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

Blood
Transient eosinophilia, leukopenia, neutropenia, hemolytic anemia, and thrombocytopenia have been reported. Some individuals, particularly those with azotemia, may develop positive direct Coombs tests during therapy with MEFOXIN*.

Liver Function
Transient elevations in SGOT, SGPT, serum LDH, and serum alkaline phosphatase have been reported.

Kidney
Elevations in serum creatinine and/or blood urea nitrogen levels have been observed. As with the cephalosporins, acute renal failure has been reported rarely. The role of MEFOXIN* in changes in renal function tests is difficult to assess, since factors predisposing to prerenal azotemia or to impaired renal function have often been present.

TREATMENT OF OVERDOSE

Other than general supportive treatment, no specific antidote is known. MEFOXIN* can be eliminated by dialysis in patients with renal insufficiency.

DOSAGE AND ADMINISTRATION

TREATMENT DOSAGE

MEFOXIN* may be administered intravenously or intramuscularly when required. (See monograph for Preparation of Solution.)

Adult Dosage

The usual adult dosage is 1 g or 2 g of MEFOXIN* every 6 to 8 hours. Dosage and route of administration should be determined by severity of infection, susceptibility of the causative organisms, and condition of the patient. The usual adult dosages are shown in the Table below.

Usual Adult Dosage

Type of of infection	Daily Dosage	Frequency and Route
Uncomplicated forms* of infections such as pneumonia, urinary tract infection, soft tissue infection	3-4 g	1 g every 6-8 h I.V. or I.M.
Moderately severe or severe infections	6-8 g	1 g every 4 h or 2 g every 6-8 h I.V.
Infections commonly needing antibiotics in higher dosage (e.g. gas gangrene)	12 g	2 g every 4 h or 3 g every 6 h I.V.

*Including patients in whom bacteremia is absent or unlikely

Therapy may be started while awaiting the results of susceptibility testing.

Antibiotic therapy for group A beta-hemolytic streptococcal infections should be maintained for at least 10 days to guard against the risk of rheumatic fever or glomerulonephritis. In staphylococcal and other infections involving a collection of pus, surgical drainage should be carried out where indicated.

tion (29 of 35 patients, 82.9%) and with bowel prolapse (33 of 40 patients, 82.5%). The visceral injuries encountered are shown in Table I. Multiple organs were injured in 13 patients with omental herniation and in 12 with bowel evisceration.

There was one death. This patient had sustained a deep laceration of the right lobe of the liver and a near-total transection of the inferior vena cava. He died intraoperatively of uncontrolled hemorrhage. Postoperative complications developed in 10 of the 74 survivors. Of the 13 patients who had no major organ injury at laparotomy, only 1 had a complication of minor wound sepsis. Nine patients who were found to have organ injury at laparotomy had the following complications postoperatively: atelectasis (three), pneumonia (two), wound infection (one), wound dehiscence (one), postoperative fever (one) and intestinal obstruction (one). Thus, the incidence of complications in the negative laparotomy group was 7.7% and in the positive group was 14.5%.

Discussion

Ever since the pioneering report of Shaftan in 1960,[1] selective operative treatment for stab wounds of the abdomen has gained wide popularity. Trauma centres have adopted their own screening techniques to delineate those victims of stabbing who require operative exploration. These methods include serial clinical observation of the patients for signs of peritoneal irritation, peritoneal lavage and local wound exploration, alone or in combination.[2-8] This policy of "selective conservatism"[4] has been supported by several large series of patients with stab wounds to the abdomen.[2-4]

The mandatory indications for celiotomy for knife wounds of the abdomen, as stressed by several authors,[1-8] include evidence of uncontrolled or continuing hemorrhage, signs of peritoneal irritation and clinical or radiologic confirmation of internal organ injury. Evisceration of bowel through a knife wound has also been mentioned frequently as an indication for mandatory exploration.[2-4] The optimal management of patients with abdominal stab wounds and omental herniation, however, has not been adequately addressed in the literature. Shaftan[1] described a case of omental extrusion through a knife wound of the abdomen; the omentum was ligated and excised and the wound debrided and the patient observed closely. Thompson and associates[8] noted that all 17 of the 300 patients with abdominal stab wounds who presented with omental herniation underwent laparotomy, with a 29% incidence of negative exploration. Based on this experience, they challenged the concept of mandatory celiotomy for all patients presenting with omental prolapse through knife wounds.

To our knowledge, the first report dealing entirely with a series of patients with omental evisceration resulting from stab wounds to the abdomen was published by Granson and Donovan.[9] In this study, 100 consecutive patients were explored because of omental herniation. Sixty-nine percent were found to have major intraperitoneal injury. The authors concluded that exploration is clearly indicated under these circumstances.

Our experience lends support to this policy. Aside from the five patients who presented in shock, celiotomy was performed on the sole indication of the presence of eviscerated omentum or bowel. The number of patients in whom no major organ injury was found was small and morbidity was minimal. The nature and incidence of major organ injury and the frequency of multisystem involvement were comparable in the patients with omental herniation and those with bowel prolapse. We conclude from our data that omental prolapse or bowel evisceration, or both, consequent to an abdominal stab wound constitute mandatory indications for laparotomy.

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ROBERT A. ZELDIN, B MATH, MD, FRCS[C]

Assessing Cardiac Risk in Patients Who Undergo Noncardiac Surgical Procedures

To confirm the usefulness of the cardiac risk index published by Goldman and associates in 1977, the author did a separate, prospective study of 1140 patients over the age of 40 years who underwent noncardiac surgical procedures. Four risk categories were defined (classes I to IV, low to high risk according to Goldman's point score). Percentages of postoperative cardiac events (life-threatening cardiac complications or cardiac death) were tabulated. The incidence of cardiac events for each risk category, classes I to IV, was 0.7%, 3%, 15% and 30%, respectively. Comparisons with Goldman's original study demonstrate that the cardiac risk index is a reliable, objective and valid method of assessing cardiac risk in patients who undergo elective surgery.

Afin de confirmer l'utilité de l'indice de risque cardiaque publié par Goldman et collaborateurs en 1977, l'auteur a réalisé une étude prospective indépendante portant sur 1140 patients de plus de 40 ans, soumis à une intervention chirurgicale autre que cardiaque. Quatre classes de risque ont été définies (les classes de I à IV correspondant à un risque de faible à élevé selon le système de cote de Goldman). Le pourcentage des incidents cardiaques postopératoires (les complications cardiaques menaçant le pronostic vital ou entraînant la mort) a été compilé. La fréquence des incidents cardiaques pour chacune des catégories de risque a été de 0.7%, 3%, 15% et 30% pour chacune des classes de I à IV respectivement. La comparaison avec l'étude originale de Goldman démontre que l'index de risque cardiaque est une méthode sûre, objective et valable d'évaluer le risque cardiaque chez les patients qui doivent subir une opération non urgente.

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In the past, preoperative assessment of surgical risk was formulated subjectively, using the American Society of Anesthesiologists' classification of physical status.[1-3] In 1977, Goldman and associates[4,5] reported a multifactorial approach to predict cardiac risk in noncardiac surgical procedures. They were able to compute objectively a cardiac risk index or score for each patient and classify that patient into an appropriate risk category, and then to observe the outcome. The present study extends their work to a separate, prospective cohort. Its purpose is to classify patients according to their cardiac risk index, observe their course and test the model as a predictor of postoperative cardiac outcome.

Patients and Methods

As a resident in surgery from July 1978 to June 1982, I was able to study all patients under my direct care. Patients included in the study sample are those for whom I was the operating surgeon or the first assistant, responsible for the patients' pre- and postoperative care at Mount Sinai, Toronto East General, Toronto General and Toronto Western hospitals. Every patient over 40 years of age admitted to the general, vascular and thoracic (noncardiac) surgery services in which I worked was available for study. Only those patients who had general anesthesia were included; uncomplicated endoscopies were excluded. In all, 1140 patients were studied. There were 870 patients with general surgical problems (abdominal, pelvic, breast, head and neck, soft tissue), 185 patients with thoracic noncardiac problems and 85 patients with vascular disease (aortic, peripheral vascular). Women accounted for 54% and men for 46% of the study population.

The nine risk factors identified by Goldman and associates[4] are listed in Table I as are the corresponding points they assigned to develop a cardiac risk index. Using the same criteria, I filled in a data sheet (Fig. 1) for each patient

Table I—Computation of the Cardiac Risk Index after Goldman and Associates[5]

Risk factor	Points
Age > 70 yr	5
Myocardial infarction in previous 6 mo	10
S_3 gallop or jugular venous distension	11
Important valvular aortic stenosis	3
Rhythm other than sinus or premature atrial contractions on last preoperative electrocardiogram	7
> 5 premature ventricular contractions/min documented at any time before operation	7
Operation — intraperitoneal, intrathoracic, aortic	3
Emergency procedure	4
General medical status (Po_2 < 60 or Pco_2 > 50 mm Hg, K < 3.0 or HCO_3 < 20 mmol/L, BUN > 17.9 mmol/L urea or Creat > 265 μmol/L, abnormal SGOT level, signs of chronic liver disease, bedridden from noncardiac causes)	3

CARDIAC RISK INDEX

Name: _____ Date: _____
ID#: _____ Attending Surgeon: _____

DATA BASE

		Data	Score
1.	Age, yr [5]		
2.	Has patient had MI within last 6 mo? [10]		
3.	S_3 gallop present? [11]*		
4.	JVD significant? [11]*		
5.	Significant aortic stenosis? [3]		
6.	Last ECG rhythm? (1 = NSR, 2 = PAC's, 3 = any other) [7]		
7.	> 5 PVC's/min at any time? [7]		
8.	Thoracotomy or laparotomy or other? [3]		
9.	Is this an emergency operation? [4]		

*If both items positive, score 11 points only once.

GENERAL MEDICAL DATA [score 3 if any values abnormal]

10.	PCO_2 (> 50 mm Hg)		
11.	PO_2 (< 60 mm Hg)		
12.	Bicarbonate (< 20 mmol/L)		
13.	Potassium (< 3 mmol/L)		
14.	BUN (> 17.9 mmol/L urea)		
15.	Creatinine (> 265 μmol/L)		
16.	SGOT (elevated)		
17.	Clinical evidence of liver disease (yes/no)		
18.	Bedridden from noncardiac causes (yes/no)		
	TOTAL SCORE		

Class (I = 5, II = 6-12, III = 13-25, IV = 26-53) ☐

FIG. 1—Data sheet for computing risk score and category. MI = myocardial infarction, JVD = jugular venous distension, ECG = electrocardiographic, NSR = normal sinus rhythm, PAC's = premature atrial contractions, PVC's = premature ventricular contractions.

preoperatively. Postoperatively, if a patient had any clinical evidence to suggest a cardiac problem, then a single electrocardiogram or serial electrocardiograms were obtained. Similar criteria for interpreting the electrocardiogram were used. Cardiac enzyme levels were determined if there was any suggestion of myocardial infarction. When the condition was not clear, medical or cardiologic consultations were obtained. Each patient was seen daily through the hospital stay. The same definitions for postoperative cardiac events that Goldman used were employed in this study.

Postoperative outcomes were classified as follows: (a) no or minor cardiac complication or noncardiac death; (b) life-threatening cardiac complication and (c) cardiac death. The life-threatening cardiac complications were cardiogenic pulmonary edema, myocardial infarction and witnessed ventricular tachycardia. A cardiac death was diagnosed if the patient died from an arrhythmia or refractory low-output state. Excluded were low cardiac-output states associated with a primarily noncardiac condition such as sepsis or respiratory failure. A noncardiac death is one from a cause other than that causing a cardiac death. Total cardiac events are represented by the sum of items (b) and (c).

Proportional analysis was used to measure statistical significance between cardiac risk classes. With the use of the central limit theorem, the normal approximation to the binomial distribution was obtained.

Results

The patients were classified into the four risk categories, classes I to IV, according to the point score from Goldman's nine risk factors (Table I): class I patients scored 0 to 5; class II, 6 to 12; class III, 13 to 25; and class IV, 26 to 53.

Table II shows the categories and outcome of the patients postoperatively. The percentage of cardiac events increased as the risk class increased. In class I patients, 0.7% had some sort of cardiac event. For classes II, III and IV, the percentages rose to 3%, 15% and 30%, respectively. Overall, 35 (3%) of the 1140 patients suffered a cardiac event.

The differences in incidence of cardiac events between risk classes in this study were significant ($p < 0.02$) for classes I and II and classes II and III. While there was a numerical difference between classes III and IV (15% v. 30%), the smaller numbers in each group made it difficult to attach significance to the difference. Closer study of the 23 class IV patients revealed that they accounted for 7 (20%) of the 35 patients suffering a cardiac event, and 6 of these were fatal complications. Thus, 43% of the cardiac deaths were in class IV patients.

The outcome for patients in the series reported by Goldman and colleagues is reviewed in Table III.[4] Both studies had a large and similar number of patients (1001 in Goldman's study and 1140 in this study). It is quite evident that Goldman had far more class III patients (130 v. 74) but fewer class II patients (316 v. 453). The incidence of cardiac events in Goldman's series was 0.9%, 6%, 14% and 78% for classes I to IV, respectively. Overall, the percentage of cardiac events in Goldman's study was 6% (58 of 1001) compared with 3% in this study.

Table II—Cardiac Risk Index — Postoperative Outcome

Class	No.	No, minor or noncardiac complication, no. (%)	Life-threatening complication, no. (%)	Cardiac death, no. (%)
I	590	586 (99.3)	3 (0.5)	1 (0.2)
II	453	440 (97)	9 (2)	4 (1)
III	74	63 (85)	8 (11)	3 (4)
IV	23	16 (70)	1 (4)	6 (26)
	1140	1105 (97)	21 (1.8)	14 (1.2)

Table III—Cardiac Risk Index — Postoperative Outcome in the Series of Goldman and Colleagues[5]

Class	No.	No, minor or noncardiac complication, no. (%)	Life-threatening complication, no. (%)	Cardiac death, no. (%)
I	537	532 (99.1)	4 (0.7)	1 (0.2)
II	316	295 (93)	16 (5)	5 (2)
III	130	112 (86)	15 (12)	3 (2)
IV	18	4 (22)	4 (22)	10 (56)
	1001	943 (94.2)	39 (3.9)	19 (1.9)

Discussion

This prospective study was designed to match that of Goldman and associates as closely as possible. In doing so its validity could be tested. Given the model Goldman proposed, one could study a new, separate patient population and observe the model's value in predicting outcome for this new group.

Part of the difference between class IV patients in the two studies can be explained by the small number of patients in this class. Moreover, as a result of Goldman's work, awareness of the high cardiac risk of class IV patients was increased and may have led to better pre- and postoperative care, thus reducing the number of cardiac events in this group.

In reviewing the current status of cardiac risk factor assessment in noncardiac surgical patients, Rose and associates[6] cited Goldman's risk factors several times. Although none of his risk factors are disputed, some authors[7-9] have included risk factors that Goldman found were not significant. Goldman's figures did not include autopsy data so the incidence of postoperative cardiac death could, in fact, be higher. I used only Goldman's risk factors as predictors but also used autopsy results when they were available.

Norman,[10] in 1978, called for the assessment of tests of predictive indices in new, subsequent studies. My study has accomplished this. Norman also pointed out that bias may be introduced towards better patient care in assessing these risk factors. This may well be the reason for the lower incidence of postoperative cardiac events in this series. Certainly the patients have benefited if such a bias existed.

Conclusions

Assessing cardiac risk using Goldman's multifactorial index is a rapid and objective method of identifying the degree of risk in patients about to undergo noncardiac surgical procedures. The present study confirms the findings of Goldman and colleagues and demonstrates the validity of their study. The cardiac risk index can easily become part of the medical record for any noncardiac surgical patient over the age of 40 years.

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Editorial note.—Dr. Zeldin examines and reaffirms the usefulness of the Goldman cardiac risk index, originally published in 1977, by studying a number of patients who underwent noncardiac surgical procedures, assessing the cardiac risk factors, using Goldman's multifactorial index. Although the results of this prospective study are similar to those of Goldman's original findings, Zeldin was unable to demonstrate that all four groups were statistically separate and distinct. His study shows that predictive tests such as Goldman's need to be assessed under different conditions. It emphasizes the need to review carefully each patient's cardiac history for possible complications so that appropriate precautions can be taken. The data collection sheet for estimating the cardiac risk index (Fig. 1) is informative should another centre wish to undergo a similar trial. Although Zeldin's study may not be original, it is reliable, has scientific importance and points the way towards assessment of one facet of risk for patients who undergo elective surgery.

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Seasonal Frequency of Testicular Torsion

The hypothesis that testicular torsion is more common in winter was examined in a retrospective survey of admissions to three Calgary hospitals. No seasonal peak in incidence of cases of torsion was identified from 1966 to 1982.

L'hypothèse voulant qu'une torsion testiculaire soit plus fréquente en hiver a été évaluée lors d'une enquête rétrospective des hospitalisations dans trois établissements de Calgary. Aucun pic saisonnier n'a été identifié dans la fréquence des torsions survenues entre 1966 et 1982.

In a series of 46 cases of testicular torsion in Dublin, Ireland, 40 occurred when the ambient temperature was less than 2°C. This finding suggested to Shukla and associates[1] that torsion of the testis was causally related to cold-induced contraction of the cremaster muscle. I have reviewed all cases of testicular torsion in Calgary, Alberta from 1966 to 1982, but found no evidence to support this hypothesis.

Patients and Results

Yearly diagnostic indices provided by the Professional Activity Study (Commission on Professional and Hospital Activities, Ann Arbor, Mich.) for three Calgary hospitals were examined for the diagnostic coding "testicular torsion" for 1966 to 1982 inclusive and for the month of discharge from hospital. Actual patient records were reviewed at random to assess the accuracy of the diagnostic coding on discharge. Two hundred and seventy-two cases of testicular torsion were identified by the procedure outlined. Review of a random 26 patient records revealed 24 patients in whom the discharge diagnosis had been confirmed surgically. In two patients, no operation was done and there was doubt as to the accuracy of the diagnosis. This sample indicates an upper confidence limit of the error rate in the overall population of less than 25% ($p = 0.05$, binomial expansion), which might be expected after considering the acute presentation and most likely therapy for this condition.

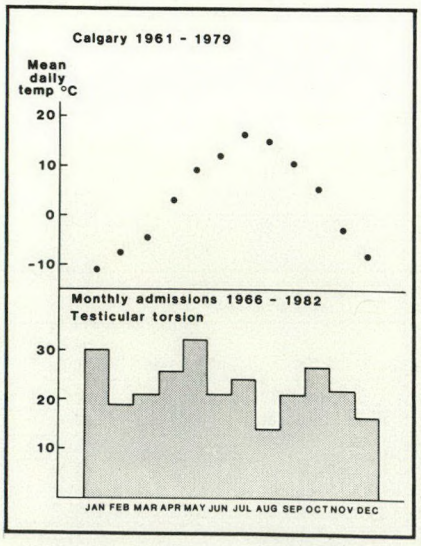

FIG. 1—Monthly frequency of testicular torsion for period 1966 to 1982 and mean daily temperature in Calgary, Alberta from 1961 to 1979 inclusive.

The duration of hospital stay for these 26 patients ranged from 4 to 29 days (mean 6 days), confirming that the month of discharge provides a reasonably accurate estimate of the date the torsion occurred.

The month of discharge for the total group of 272 cases is shown graphically in Fig. 1, which also provides the mean daily temperature for each month for Calgary from 1941 to 1979.[2] Using Hewitt's rank-sum criterion of seasonality,[3] no significant difference in the frequency of torsion was found either for the 6 coldest months or any other sequential 6-month period (for November to April inclusive, rank sum 40, $p = 0.5$). No seasonal trend was apparent when the data were manipulated in other ways; in particular, separating adults from children (16 years or younger) caused no change in the pattern.

Discussion

Torsion of the testis is uncommon, but this has not restricted speculation as to its cause. Most authorities[4-6] have concentrated on predisposing anatomical variations, including abnormal reflection of the tunica vaginalis upon the testicle, complete tunica vaginalis investment of the testicle and cord (bell-clapper deformity), an elongated mesorchium and separation of the epididymis from the testicle. On this basis it has been suggested that the other testicle is also at risk for torsion, presumably because of similar minor malformations. Torsion has been recorded as more likely in cryptorchidism,[7] especially when associated with malignant degeneration.[8] Others have commented on an association between torsion and violent exercise or even trauma to the testicle.[9]

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In 1912, Uffreduzzi (quoted by Harrison[5]) suggested that one cause of torsion was contraction of the cremaster muscle when subjected to a stimulus such as sudden cold. This idea was supported by an experimental study of the distribution of cremaster by Muschat,[10] who showed a spiral insertion of the muscle which could conceivably contribute to rotation of the testis under some conditions. A similar etiology was proposed by Donohue and Utley.[11] Shukla and associates[1] found evidence for a seasonal incidence of torsion in Dublin and related this to an ambient temperature of 2°C or lower. Two subsequent series, reported briefly from centres in the United Kingdom,[12,13] offered support for a seasonal incidence of torsion.[14]

Because there are greater extremes of daily temperature in much of Canada than in the British Isles, it is appropriate to examine the frequency of testicular torsion under such conditions. The hypothesis for a peak incidence in cold weather might find even more support under extremes of climate. However, no evidence was found to support a seasonal frequency for torsion among a series of 272 cases identified retrospectively in Calgary, Alberta.

The reason for the difference between these results and those from the three series reported from the United Kingdom and Ireland is not clear. It seems unlikely that using the hospital discharge date rather than the date of occurrence of torsion would obscure any significant seasonal trend. A more important criticism of this kind of retrospective study would be the rate of error in the diagnosis at discharge. In testicular torsion, the admission diagnosis might be expected to have a high rate of error (because of confusion with acute epididymitis and other conditions) but it appears likely that physicians would provide a fairly accurate discharge diagnosis for this relatively simple disease state. This is supported by the finding in this series that in 24 of the 26 patient records examined at random, the diagnosis was confirmed at operation. Perhaps other series should be examined under different climatic conditions before the seasonal hypothesis is rejected.

I thank the Directors of Surgery in Alberta Children's Provincial General Hospital, Calgary General Hospital and Foothills Hospital, Calgary, for access to patient records.

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Acute Hemorrhagic Pancreatitis and Diabetes Mellitus following Endoscopic Retrograde Cholangiopancreatography

Endoscopic retrograde cholangiopancreatography (ERCP) is generally regarded as a safe and useful investigation in the diagnosis and management of diseases of the pancreas and biliary tree. Asymptomatic hyperamylasemia is not uncommon following this procedure, but clinical pancreatitis is rare. The authors report on a 56-year-old man who suffered life-threatening acute hemorrhagic pancreatitis 2 weeks after ERCP was performed for the investigation of abdominal pain. He subsequently had insulin-dependent diabetes mellitus, which was not present at the time of ERCP.

La cholangiopancréatographie endoscopique rétrograde (CPER) est généralement considérée comme une procédure sûre et utile pour le diagnostic et le traitement des maladies du pancréas et de l'arbre biliaire. Après cette intervention, l'hyperamylasémie n'est pas rare mais la pancréatite franche est rare. Les auteurs signalent le cas d'un homme de 56 ans qui a souffert d'une pancréatite hémorragique aiguë ayant menacé le pronostic vital, 2 semaines après une CPER pratiquée pour diagnostiquer les causes d'une douleur abdominale. Il a par la suite souffert d'un diabète insulino-dépendant qui n'existait pas au moment de la CPER.

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Endoscopic retrograde cholangiopancreatography (ERCP) is frequently used in the diagnosis and management of diseases of the pancreas and biliary tree. Asymptomatic hyperamylasemia is a common sequela, but serious complications are considered to be rare.[1-7] We recently encountered a case of life-threatening acute hemorrhagic pancreatitis following ERCP performed for the investigation of abdominal pain. The examination showed that the ducts were normal, but within days an acute abdomen developed, and hemorrhagic pancreatitis was present at laparotomy. The patient recovered but subsequently insulin-dependent diabetes mellitus developed.

Case Report

Nine years before the presenting illness, our patient, a 56-year-old white man, had undergone cholecystectomy for cholelithiasis, following which he had recurrent episodes of ascending cholangitis due to a bile-duct stricture. Endoscopic retrograde cholangiopancreatography was performed; it showed a stric-

ture of the common bile duct at the level of the cystic duct, retained irregular stones in the distal common bile duct and normal-appearing pancreatic ducts. A choledochoenterostomy was performed. He remained afebrile and with no symptoms suggestive of common-duct obstruction for 8 years. Then he began to suffer episodes of sharp epigastric pain, aggravated within 30 minutes by food and relieved by antacids and cimetidine. He had mild hypertension that was controlled by propranolol 40 mg twice daily. Because of the frequent episodes of pain, a second ERCP was performed at the University of Alberta Hospital. The pancreatic duct was cannulated and visualized over approximately 21 cm; the main duct and the secondary radicals appeared normal and no areas of narrowing were seen. An attempt was made to cannulate the common bile duct, but only a small amount of dye was seen in the proximal 2 cm; this portion of the common duct appeared normal in calibre.

Following ERCP the patient returned home 500 km away. He was well for 2 weeks after the ERCP but then he experienced epigastric and left upper quadrant pain. The pain was severe and became progressively worse; it was associated with distension but there was no vomiting. He was admitted to his local hospital. There his abdomen was noted to be tender, without guarding or rebound tenderness. His oral temperature was 38°C. Plain abdominal roentgenograms indicated an ileus. He was treated by nasogastric suction and fluids, ampicillin and cimetidine given intravenously. Ascites was present and the amylase level of the tapped fluid was increased to 135 U/L, when the serum amylase level was normal. The urinary amylase-creatinine ratio was 3:100. The hemoglobin value was 120 g/L. A trace of blood was apparent in the nasogastric aspirate. Two units of blood were transfused. After initial improvement he rapidly deteriorated and his pain, distension and ascites became worse. Twelve hours later he was transferred to the University of Alberta Hospital.

On admission he appeared acutely ill; the pulse rate was 88 beats/min, blood pressure 140/80 mm Hg, respiratory rate 30/min and oral temperature 36.9°C. There was no jaundice; his abdomen was distended and there was shifting dullness and hypoactive bowel sounds. There was marked, diffuse tenderness with guarding and rebound tenderness in all four quadrants. The nasogastric tube was draining bile-stained material but no blood. The leukocyte count was 14.6×10^9/L with 30% polymorphonuclear band cells. The hemoglobin level was 120 g/L, serum amylase level 40 U/L and blood glucose 11.9 mmol/L. The blood glucose was previously normal and the hemoglobin 3 years previously was 170 g/L. The serum electrolyte values were normal; on room air the partial pressure of oxygen in venous blood was 57 mm Hg, and of carbon dioxide was 37 mm Hg, and the pH was 7.49. Abdominal ultrasonography demonstrated normal biliary ducts, but the pancreas could not be visualized because of overlying gas-containing bowel loops. A perforated viscus was suspected. At laparotomy, the abdomen contained 2 L of clotted and fresh blood. The pancreas was about three times the normal size. The diagnosis was hemorrhagic pancreatitis with bleeding into the peritoneal cavity. No abnormality was detected in the common bile duct. The blood was evacuated and the abdomen was lavaged with saline.

Recovery was slow. The blood glucose levels were persistently elevated and the patient required insulin, 10 units regular plus 12 units lente every morning. He is now able to eat without pain and his bowel habit has remained normal with no appearance or characteristic suggestive of steatorrhea.

Discussion

Complications following ERCP are few and usually mild. In one third of patients, benign hyperamylasemia or hyperamylasuria will develop 1 or 2 days following ERCP, but injection pancreatitis with pain, fever and leukocytosis is unusual.[1-7] When this does occur, it usually is seen 24 to 36 hours following the ERCP, not 2 weeks later as occurred in our patient. Injection pancreatitis may occur more commonly in inexperienced hands, but this was not true of our endoscopist. There was nothing unusual in the amount of dye used for the injection, the pressure applied or the rate of injection. Furthermore, the pancreatic ducts visualized by ERCP were normal.

There was no obvious cause of the hemorrhagic pancreatitis other than the ERCP. The only medication the patient had been taking was propranolol for hypertension. He had been under treatment with this agent for 8 years; propranolol is not thought to be associated with the development of severe pancreatitis.[8] He had not been taking thiazides, and his serum lipid and calcium levels were not known to be elevated. No stones were detected in the common duct by ERCP or ultrasonography or at operation.

We thank Dr. A. Kenyon for referring the patient, Dr. S. Adams for reviewing the ERCP films and Mrs. Jackie Polovick for typing the manuscript.

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SESAP IV Critique

ITEM 17

The procedure depicted is a parietal cell vagotomy (proximal gastric vagotomy, super-selective vagotomy). Most surgeons who use it do so as a definitive operation for peptic ulcer disease, without pyloroplasty or bypass of the pylorus, which seems to be its chief advantage. It has not been associated with many of the postoperative complications of operative procedures that destroy or bypass the pylorus. Parietal cell vagotomy has not ordinarily been considered appropriate for patients with gastroesophageal reflux. Some investigators do use this procedure for patients with hemorrhage, obstruction, or perforation from peptic ulcer. Latarjet described the anatomy of the vagus nerves, on which this operation is based, some 60 years ago.

D

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Refresher Course in Genitourinary Radiology

The biannual Refresher Course in Genitourinary Radiology, offered by the University of Toronto, will be held Oct. 18 and 19, 1984 at the Mount Sinai Hospital, Toronto, Ont. This course will deal with recent advances in genitourinary imaging and will review selected areas of general interest. Topics will include digital subtraction angiography, computed tomography, ultrasonography, nuclear magnetic resonance, nuclear imaging, interventional techniques and the investigation of impotence.

For further information contact Dr. Robin R. Gray, Course Director, Department of Radiology, The Wellesley Hospital, 160 Wellesley St. E, Toronto, Ont. M4Y 1J3 or call (416) 966-6810.

Practical Hand Surgery

The 14th annual meeting of the American Association for Hand Surgery will be held in conjunction with the Mexican Society for Surgery of the Hand and the Caribbean Society for Hand Surgery, Nov. 25–28, 1984 at the Acapulco Princess Hotel, Acapulco, Mexico.

The theme for this year's meeting will be the management of practical problems of hand surgery. Emphasis will be on cost effectiveness of accurate, quality, hand surgery care.

For further information contact Dr. Robert J. Demuth, Central Office, American Association for Hand Surgery, 2564 Branch St., Middleton, Wisc. 53562, USA.

International Meeting on Vascular Pathology

The 14th International Meeting on Vascular Pathology will he held Oct. 22–24, 1984 at the Auditorium of the University of Coimbra, Coimbra, Portugal. It has been organized by the Department of Surgical Pathology, University of Coimbra, and sponsored by the International Union of Angiology.

For further information contact Mario Blanco Peres, Rua Gonçalo Cristóvão, 116-3°, 4000 Porto, Portugal.

CLASSIFIED ADVERTISING

As a further service to its readers the *Canadian Journal of Surgery* is pleased to accept suitable classified advertisements. The deadline is 1 month before issue date. Regular classified rates (for each insertion): $35.00 for the first 40 words or less, additional words 35¢ each (additional $13.00 for frame). Special Display under 75 words, 2 1/4″ × 2″ $85.00. $5.00 charge (first insertion only) for CJS box numbers. Display rates available on request.

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—S84-019

CANADIAN JOURNAL OF SURGERY

Publication and deadline dates for 1984:

January,	1984	– December	1,	1983
March	"	– February	1,	1984
May	"	– April	1	"
July	"	– June	1	"
September	"	– August	1	"
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